PROSPECTIVE, RANDOMISED COMPARATIVE STUDY ON EFFECTS OF ADDING DEXMEDETOMIDINE AND FENTANYL TO EPIDURAL BUPIVACAINE ON POSTOPERATIVE ANALGESIA IN PATIENTS UNDERGOING THORACOTOMY

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CERTIFICATE

This is to certify that the dissertation entitled, **"PROSPECTIVE, RANDOMISED COMPARATIVE STUDY ON EFFECTS OF ADDING DEXMEDETOMIDINE AND FENTANYL TO EPIDURAL BUPIVACAINE ON POSTOPERATIVE ANALGESIA IN PATIENTS UNDERGOING THORACOTOMY",** submitted by **Dr. M. THIRILOGA SUNDARY** in partial fulfilment for the award of the degree of Doctor of Medicine in Anaesthesiology by the Tamilnadu Dr. M.G.R. Medical University, Chennai is a bonafide record of the work done by her in the Institute of Anaesthesiology and Critical Care, Madras Medical College, Chennai during the academic years 2010-2013.

Dr.M.Vasanthi,M.D.,D.A.,DNB.,
Professor and Director,
Institute of Anaesthesiology
& Critical Care,
Madras Medical College,
Chennai - 600003.

Dr.V.Kanagasabai,M.D.,
Dean,
Madras Medical College
& Rajiv Gandhi Govt.
General Hospital,
Chennai – 600003.

DECLARATION

I solemnly declare that this dissertation entitled **"PROSPECTIVE, RANDOMISED COMPARATIVE STUDY ON EFFECTS OF ADDING DEXMEDETOMIDINE AND FENTANYL TO EPIDURAL BUPIVACAINE ON POSTOPERATIVE ANALGESIA IN PATIENTS UNDERGOING THORACOTOMY"** has been prepared by me, under the Guidance of **Prof. Dr. SAMUEL PRABHAKARAN, M.D.,** Associate Professor of Anaesthesiology, Institute of Anaesthesiology and Critical Care, Madras Medical College, Chennai in partial fulfilment of the regulations for the award of the degree of M.D. [Anaesthesiology], examination to be held in April 2013. This study was conducted at Institute of Anaesthesiology and Critical Care, Madras Medical College, Chennai. I have not submitted this dissertation previously to any university for the award of any degree or diploma.

Date:

Place: Chennai **Dr. M. THIRILOGA SUNDARY**

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ABBREVATIONS

PR	-	Pulse Rate
HR	-	Heart Rate
SBP	-	Systolic Blood Pressure
DBP	-	Diastolic Blood Pressure
MAP	-	Mean Arterial Pressure
VAS	-	Visual Analogue Score
SpO_2	-	Oxygen Saturation
PCA	-	Patient Controlled Analgesia
BIS	-	Bispectral Index
i.v.	-	intravenous
ASA	-	American Society of Anesthesiologists
RR	-	Respiratory Rate
S.D.	-	Standard Deviation

CONTENTS

INTRODUCTION

Thoracotomy is one of the most painful surgeries. Post thoracotomy pain leads to delayed recovery and contributes to postoperative morbidity in a highly significant manner[9]. Acute pain on the site of incision alters chest wall mechanics and impedes effective expansion of the chest, cough and ability to clear secretions predisposing the patients to delayed recovery, respiratory infection, ventilation perfusion mismatch and hypoxemia due to atelectasis[9]. Optimum pain relief after thoracotomy is necessary in order to reduce the incidence of atelectasis and postoperative pneumonia[3]. Epidural analgesia has emerged to be the gold standard analgesic technique for the management of postoperative pain after thoracotomy[19].

It was Sicard and Cathelin who first reported epidural anaesthesia in 1901. Epidural needle was first introduced by Tuohy in 1945, which is widely used now. The first epidural catheter was introduced by Eugene Aburel. He used a ureteral catheter made of silk into the epidural space for labour analgesia and in 1962, after several

modifications, the first polyvinyl catheter was introduced in the epidural space, thus facilitating continuous epidural block. Efficacy of adding opioids into the epidural space was first published by Behar et al in 1979 in the journal 'The Lancet'. Today, epidural has become a part of routine regimen for intra- and post- operative pain relief.

When an adjuvant like an opioid (fentanyl) is added to a local anaesthetic such as bupivacaine, its concentration can be decreased to 0.125 % or even 0.0625% instead of 0.5% or 0.25%. This would decrease the incidence of hypotension and unwanted motor blockade[16].

Dexmedetomidine is a highly selective newer prototype of α-2 agonists with α2:α1 selectivity of approximately 8 times more in comparison to clonidine[4]. Addition of dexmedetomidine to local anaesthetic provides early onset of sensory block, adequate sedation and a prolonged postoperative pain relief[14].

This study was undertaken to compare the effects of adding dexmedetomidine and fentanyl to epidural bupivacaine on post thoracotomy pain characteristics.

AIM OF THE STUDY

1. To compare the duration and quality of post operative analgesia between fentanyl and dexmedetomidine when added epidurally to bupivacaine in patients undergoing thoracotomy.
2. To evaluate hemodynamic changes between the two groups, sedation and adverse effects, if any.

POST THORACOTOMY PAIN

INTRODUCTION:

Thoracotomy requires a very painful, muscle splitting incision that is subject to continuous motion as the patient breathes. The reason for severe pain after thoracotomy is due to retraction, resection or fracture of ribs, splitting of muscles like lattissimus dorsi, serratus anterior, pectoralis major and the intercostal muscles, dislocation of costovertebral joints, irritation of pleura by intercostal drainage tubes and injury to intercostals nerves[23].

Suboptimal management of pain after thoracotomy has major respiratory consequences [24]. Inspiration is limited by pain, leading to reflex contraction of expiratory muscles, subsequently leading to decreased functional residual capacity, atelectasis, shunting and hypoxemia. Moreover, since deep breathing requires stretching of the incision site, patients without adequate pain relief try to prevent stretching of the incision by contracting their expiratory muscles i.e., splinting, so as to limit the stretch occurring at the incision during inspiration. This failure to take a deep

breath before exhaling forcefully results in ineffective cough leading to retention of secretions, atelectasis and pneumonia leading to respiratory failure. Other complications of inadequate pain relief include reduced mobility leading to deep vein thrombosis and pulmonary embolism. Acute pain also leads to increased sympathetic tone causing increased after load and myocardial dysfunction and arrhythmia.

ANALGESIC OPTIONS AVAILABLE:

When no contraindication exists, central neuraxial or regional analgesia (epidural, intrathecal and paravertebral) is the technique of choice. If contraindication is present due to anatomical difficulties or systemic or local infection then parenteral opioid infusion is the technique of choice.

PARENTERAL OPIOIDS:

Although reasonably good analgesia can be achieved by this technique, it is not usually the technique of choice as it can lead to respiratory depression and inhibition of cough reflex which is not favourable after thoracotomy.

Further, immediately after surgery the patients are drowsy to use the PCA pump on their own.

EPIDURAL ANALGESIA:

It is considered to be the gold standard for pain management after thoracotomy. Usually the catheter is placed at the level of midpoint corresponding to the dermatome level of skin incision. The epidural drug is usually administered by a continuous infusion, patient controlled epidural analgesia (PCEA) or a combination of the two. The drawbacks include significant failure rate even in experienced hands and technical difficulty due to caudal angulations of the spinal process at the thoracic level.

INTRATHECAL OPIOIDS:

Preservative free opioids introduced into subarachnoid space produce analgesia by moving cephalad to the site of injection depending on the baricity and volume, strength and the nature of the opioid. Opioids with lower lipid solubility like morphine migrate cephalic more readily before penetrating the spinal cord. The delay in the onset

of analgesia after intrathecal injection is usually by 1 to 2 hours.

The drawback of using intrathecal opioid is usually sedation and respiratory depression due to excessive rostral spread. All patients require monitoring for respiration and degree of sedation for at least 24 hours. Other side effects include pruritus, nausea and vomiting and urinary retention.

PARAVERTEBRAL BLOCK:

Paravertebral space is a wedge shaped area lateral to the intervertebral foramen and it communicates above and below with paravertebral spaces. The intercostal nerve passes through the space without a facial sheath and hence reliably blocked with a local anaesthetic. The term extrapleural blockade has been used synonymously with the paravertebral block as the nerve lies outside the parietal pleura. This technique can be used as a single shot or as a continuous infusion with a catheter placed via a tuohy needle. Plain local anaesthetic solutions like bupivacaine 0.25% is used at a rate of 10-15ml/hour. The advantage of this blockade is that the motor and sympathetic block are

unilateral with less hypotension and better preserved respiratory function when compared to epidural blockade.

INTERCOSTAL NERVE BLOCK:

They are usually performed by single injections two or three intercostal spaces above and below the level of incision. They provide localized analgesia without any sympathetic blockade. It usually requires multiple injections and is usually short acting and the analgesia is inadequate posteriorly as the intercostal nerve gives off a branch posteriorly and the block is usually performed anterior to this. Local anaesthetic toxicity can be a problem as it usually requires multiple injections and large volume of local anaesthetic.

INTERPLEURAL ANALGESIA:

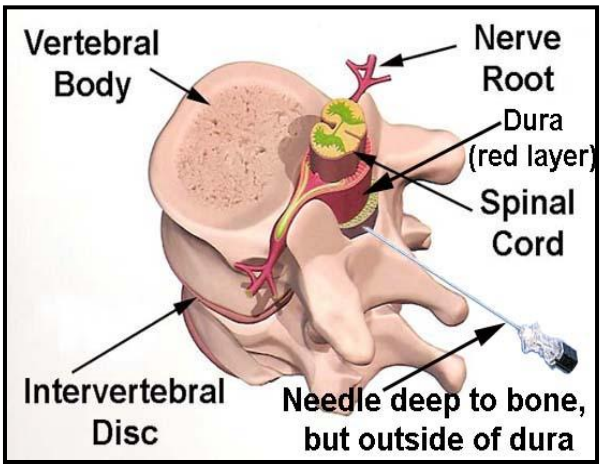
In this technique the local anaesthetic is usually injected between the parietal and visceral pleura either as a single bolus or as an infusion via indwelling catheter. The disadvantage includes pooling of local anaesthetic in dependent position and loss of local anaesthetic via chest drain limiting effectiveness.

CRYOPROBE NEUROLYSIS:

This technique involves application of low temperature probe to intercostal nerves to destroy them to provide long lasting analgesia up to 3 months until the nerves grow back by axonal regeneration. Complications include neuralgia and paresthesia and hence rarely used in practice now.

EPIDURAL BLOCK

Epidural blockade[5] has a unique feature of segmental blockade where by only the desired segments required for analgesia are blocked, unlike the uncontrolled level of blockade which happens in spinal anaesthesia. The period of analgesia can be extended in the post-operative period through continuous catheters.



ANATOMY OF EPIDURAL SPACE:

Epidural space is an anatomical compartment in the vertebral column that extends from the base of the skull to the sacral hiatus, between the dural sheath and the spinal canal. In some areas it is a real space whereas in others it is a potential space.

The boundaries of the epidural space are as follows:

- **Superiorly -** fusion of the spinal and periosteal layers of the dura mater at the foramen magnum.
- **Inferiorly -** sacrococcygeal membrane
- **Anteriorly -** posterior longitudinal ligament, vertebral bodies and disc.
- **Laterally -** pedicles and intervertebral foramina.
- **Posteriorly -** ligamentum flavum, capsule of facet joints and laminae.

The epidural space is most roomy at the upper thoracic levels. In adults the epidural space measures 0.4mm at C_7 –T_1 region, 7.5mm in the upper thoracic region, 4.1mm at T_{11} – T_{12} region and 4 – 7mm in the lumbar region.

CONTENTS OF EPIDURAL SPACE:

Epidural space is a potential space filled with the fat, lymphatics, veins, and nerve roots that traverse it, areolar tissue. It has no free fluid. 31 pairs of spinal nerves with their dural sleeves traverse the space and pass through the intervertebral foramina.

To reach the epidural space in mid sagittal plane, the following structures are penetrated by the epidural needle:

- Skin and subcutaneous tissue
- Supraspinous ligament
- Interspinous ligament and
- Ligamentum flavum.

PHYSIOLOGICAL EFFECTS OF EPIDURAL BLOCKADE:

The physiologic effects of epidural block depend on the level of spinal segment which is blocked and also the number of spinal segments being blocked. Usually, epidural blocks given at higher thoracic levels and extensive epidural blocks covering a large number of spinal segments are associated with more sympathetic block. These have a more profound physiologic effect, especially in the cardiovascular system.

CARDIOVASCULAR SYSTEM:

The effects on the heart and blood vessels depend on the level and the degree of sympathetic blockade. The cardiovascular effects of a block above T4 are the result of a high sympathetic block. The heart is supplied by

sympathetic fibres from T_1 to T_4. When these are blocked, cardiac contractility is decreased leading to bradycardia and profound hypotension[20]. In addition to these, a high thoracic epidural blockade also causes[21,22] vasoconstriction of upper limbs and head and neck region and increased central venous pressure but there is no increase in stroke volume. Moreover secretion of catecholamines from the adrenal medulla is blocked due to splanchnic nerve blockade. Thus the normal compensatory mechanisms of a patient to decreased cardiac output are lost in sympathetic blocks above T4.

Vascular smooth muscles are innervated by sympathetic fibres from T5 to L1 which maintain the vasomotor tone. Epidural block causes bilateral sympathetic blockade of these fibres, which cause venodilation with venous pooling of blood resulting in hypotension.

RESPIRATORY SYSTEM:

Epidural blockade even up to thoracic levels have minimal effect on ventilation and oxygenation. Major alteration in pulmonary function does not occur even with

abdominal or intercostal muscle paralysis by a high thoracic block.

GASTROINTESTINAL SYSTEM:

Due to the blockade of the sympathetic splanchnic fibres from the T5 to L1 level, vagal action becomes unopposed, leading to an increase in bowel secretions, and an increased peristalsis causing a smaller, contracted gut.

RENAL SYSTEM:

Epidural block has very little effect on renal function because the renal blood flow is usually maintained. Urinary retention may occur till the block wears off.

NEUROENDOCRINE RESPONSE:

During the perioperative period, epidural block decreases the stress response to pain by decreasing the release of stress hormones like epinephrine, nor epinephrine, vasopressin.

SIDE EFFECTS:

Following are the side effects of epidural blockade:

Due to physiological changes:

- Hypotension
- Bradycardia.

Improper needle positioning:

- Post dural puncture headache.
- Inadvertent high spinal.

Others:

- Hematoma.
- Epidural abscess, Meningitis.
- Allergy to local anaesthetics, local anaesthetic toxicity.
- Anterior spinal artery syndrome.
- Arachnoiditis and Transverse myelitis.

CONTRAINDICATIONS:

Absolute

- Patient refusal.
- Coagulopathy.
- Skin infection at the injection site.

- Raised intracranial tension.
- Uncorrected hypovolemia.

Relative

- Uncooperative patients.
- Pre-existing neurological disorders.
- Fixed cardiac output states.
- Vertebral anomalies.

PHARMACOLOGY OF DEXMEDETOMIDINE

Dexmedetomidine is a selective α2-receptor agonist with evidence of an increased ratio of α2 to α1 activity of 1620:1, as compared to 220:1 when contrasted against clonidine. The mechanism by which α2-adrenergic receptor agonists produce analgesia and sedation is multifactorial.

Dexmedetomidine possesses analgesic properties and many other advantages and also lacks respiratory depression that may make it a useful and safe adjunct in diverse clinical applications.

Both hypnotic and supraspinal analgesic effects of dexmedetomidine are mediated by noradrenergic neurons, via hyperpolarisation of neurons.

MECHANISM OF ACTION:

1. Inhibition of nor epinephrine release and its associated activity in the descending medullo-spinal noradrenergic pathway.

2. Suppresses neuronal firing in the locus ceruleus. Suppression of these inhibitory controls causes release of mediators and neurotransmitters that in turn decrease the secretion of histamine and produce hypnosis without any depression of ventilation.

In addition suppression of activity along the descending noradrenergic pathway terminates propagation of pain signals, resulting in analgesia or decreased awareness of noxious stimuli.

In neurons of the superficial dorsal horn of the spinal cord, dexmedetomidine suppresses and reduces pain transmission / conduction by:

1. Inhibiting the release of glutamate and substance P from primary afferent terminals and
2. G - protein mediated activation of potassium channels causing hyperpolarisation of inter-spinal neurons. The stress response to surgery can be attenuated by sympatholytic effects caused by postsynaptic activation of central α2-recptors, leading to reductions in blood pressure and slowing of heart rate.

Epidural dexmedetomidine exhibits synergism with local anaesthetics by prolonging the sensory/motor block duration time, postoperative analgesia and results in intense motor block without any additional morbidity.

Clinical studies exhibit potentiating of neuraxial local anaesthetics, decrease in intraoperative anaesthetic requirements with prevention of intraoperative awareness, improved intraoperative oxygenation and improved postoperative analgesia when epidural dexmedetomidine was used in conjunction with general anaesthesia. No neurological deficits have been reported till date in studies on both humans and animals during intrathecal / epidural use.

PHARMACOLOGY OF FENTANYL

INTRODUCTION:

The chemical name of fentanyl is N-(1-phenyl-4-piperidyl) propionanilide. It is a structural analogue of meperidine. It is available as a citrate containing compound which does not require preservatives and is water soluble. One ml of fentanyl contains 50µg of fentanyl and 0.0785mg of citrate. The pka of fentanyl is 8.43. In the blood, 84% of the drug is bound to plasma protein. Fentanyl has a high lipophilicity with an octanol water partition coefficient of 816 at physiologic pH compared with 1.4 for morphine.

PHARMACOKINETICS OF NEURAXIAL ADMINISTRATION OF FENTANYL:

The actions of fentanyl in the epidural and intrathecal space have been well studied. After neuraxial administration it gets distributed in to the epidural space by moving across the meninges in to the CSF. Through the circulation of CSF it binds to the opioid receptors which have been identified in the spinal cord. It migrates also to supraspinal sites via the CSF. Due to its high octanol –

buffer partition coefficient it has a high vascular permeability. So some amount of systemic absorption occurs through the spinal and epidural vessels and is directly proportional to the dose of bolus dose. Uptake into non specific binding sites such as the epidural fat also occurs as it is lipophilic.

Once it enters the CSF circulation, similar to other opioids, fentanyl spreads rostrally. At the level of cervical spine, the peak CSF concentration is reached within 20 minutes compared to 3 hour for morphine. But the proportion of administered drug that migrates to the cervical region is small (10%) compared to morphine because of its high affinity to the non specific binding sites in the lipid rich spinal cord. It has been postulated that fentanyl is less likely to produce clinically significant depression of ventilatory drive than morphine. Most suggest that fentanyl is associated with less number of adverse effects like sedation, pruritus, nausea, vomiting, and urinary retention.

DOSE REQUIREMENTS:

The dosage recommendations for fentanyl for repeated single bolus administration is 1-3µg/kg, up to 5µg/kg. Onset of analgesia occurs in 15 min and lasts 2 to 4 hour.

SIDE EFFECTS:

The most common side effect with epidural fentanyl is pruritus with an incidence of 0-85%. The onset usually occurs within an hour of bolus epidural injection, is not associated with release of histamine, and lasts 20-30min. The pruritus can be antagonised with naloxone administration. It is usually localised to the head and neck region and is of reduced intensity when compared to morphine.

There has been a 20 – 30% incidence of nausea and vomiting with epidural administration of fentanyl. Nausea typically occurs within 3 hours of administration of fentanyl.

Epidural opioids react with and block opioid receptors in the sacral portion of spinal cord. This blocks

parasympathetic sacral neural outflow and cause relaxation of detrusor muscle of urinary bladder. The maximum capacity of the urinary bladder is increased, leading to urinary retention. In most studies the incidence of urinary retention is less than 12% even though the reported incidence of urinary retention is from 0 -50%.

The most serious adverse effect of the use of epidural opioids is respiratory depression. Clinically significant respiratory depression can occur with either bolus doses or continuous infusions of epidural fentanyl. The ventilatory response of the patient in response to carbon dioxide accumulation is depressed after an epidural bolus dose of 200µg. However incidences of respiratory arrests and profound respiratory depression have been reported after a 100µg dose. The overall incidence of clinically significant respiratory depression is approximately 1.8%.

PHARMACOLOGY OF BUPIVACAINE

Bupivacaine is an amide local anaesthetic agent. It belongs to the homologous series of n-alkyl substituted pipecholyl xylidines. It is produced for clinical use as a racemic mixture containing both 'S' and 'R' forms in equal proportion. It is supplied as a hydrochloride salt. Its chemical name is 1-butyl-n-(2, 6-dimethyl phenyl) -2-piperidine decarboxamide hydrochloride monohydrate.

PHYSICO-CHEMICAL PROFILE[25]:

Molecular weight	-	288
pKa	-	8.1
Plasma protein binding	-	95%
Partition coefficient	-	28 (lipid solubility)
T ½	-	210 min
Clearance	-	8.3 l/min

MECHANISM OF ACTION:

Like all the other local anaesthetics, it inhibits Na+ channels. It decreases or prevents large transient increase in permeability of the cell membranes to Na ions that

follows depolarization of the membrane and thereby blocks the nerve conduction. It also reduces the permeability of the resting nerve membrane to potassium ions as well as sodium ions and hence has got a stabilising action on all excitable membranes.

CLINICAL EFFECTS:

Local – nerve blockade

Regional – pain, temperature, touch, motor power and vasomotor tone supplied by the nerves are blocked.

Systemic – effects due to systemic absorption or accidental intravenous administration.

It is 4 times more potent than lignocaine but the onset of action is slower. The duration of action is longer. Sensory block is more marked than the motor block.

SYSTEMIC EFFECTS:

CNS:

- Circumoral numbness, metallic taste
- Tinnitus, light headedness, dizziness
- Confusion, slurred speech
- convulsions

CVS:

- Depresses automaticity and contractility of the heart.
- Slows conduction of cardiac action potential and prolongation of PR and QR intervals on ECG.
- Re-entrant phenomenon and ventricular arrhythmias.
- R-enantiomer is more toxic than S-enantiomer
- Pregnancy increases cardiotoxic effects of bupivacaine

PHARMACOKINETICS:

- Rapidly absorbed from the site of injection
- Peak systemic concentration – 5 to 30 minutes after administration
- Metabolism in liver – dealkylation to pipecoloxylidine, aromatic hydroxylation
- Excretion – 5% by kidney as unchanged drug and rest as metabolites

CONTRAINDICATIONS:

- Known hypersensitivity to amide local anaesthetics
- Intravenous regional anaesthesia(IVRA)

MAXIMAL DOSE:

2.5 mg/kg body weight and the strength used is 0.25 – 0.75% with or without adrenaline (1:200000 or 1:400000)[25]. Adrenaline does not prolong its effect, but reduces its toxicity.

REVIEW OF LITERATURE

1. Sukhminder Jit Singh Bajwa et al[1] did a study to compare the effects of dexmedetomidine and fentanyl for epidural analgesia in patients undergoing lower limb orthopaedic surgeries. They compared the effects of adding fentanyl and dexmedetomidine to epidurally administered ropivacaine on the hemodynamic status, analgesic and sedative effects. They recruited hundred patients who underwent lower limb orthopaedic surgeries in the age group 21 -56 years of both gender belonging to ASA 1-2 status. Patients were divided into two groups with 50 patients in each group–GroupRD (Ropivacaine plus dexmedetomidine) and RF (Ropivacaine plus fentanyl). Ropivacaine. Drug was injected in both the groups at a dose of 15ml (0.75% ropivacaine) along with dexmedetomidine 1µg/kg in the RD group and fentanyl 1µg/kg in the RF group. The parameters studied included cardiorespiratory, block characteristics like time to onset of analgesia at T10, maximum sensory level, time to complete motor blockade, two segmental regression time and time to first rescue analgesia. The demographic profile was comparable in both

the groups. Onset of sensory analgesia at T_{10} (7.12+2.44 vs 9.14+2.94) and establishment of motor blockade (18.16+4.52 vs 22.98+4.78) was significantly earlier in the RD group. The analgesia in the postoperative period was significantly prolonged in the RD group (366+24.42) when compared to the fentanyl group (242.16±23.86). The sedation scores were better with high incidence of dry mouth in the dexmedetomidine group. The incidence of nausea and vomiting were higher in the RF group. They concluded that dexmedetomidine is a better epidural adjuvant when compared to fentanyl as it provided stable hemodynamics, early onset of sensory anaesthesia with prolonged postoperative analgesia and better sedation levels.

2. M. Elhakim et al[2] studied the effect of epidural dexmedetomidine on intraoperative awareness and postoperative pain after one lung ventilation. They recruited 50 adult patients for the study. They were randomly assigned to receive either epidural dexmedetomidine 1µg/kg with bupivacaine 0.5% 30-40mg (group D) or bupivacaine (0.5%) 30- 40mg (group B) alone

after induction of general anaesthesia. Postoperatively pain was assessed using 11point verbal rating scale (VRS) and sedation was assessed using the inverted observers assessment of alertness/sedation scale (OAA/S). They showed that patients receiving dexmedetomidine required less supplementary fentanyl than patients in group B to maintain BIS values between 40 and 60. The verbal rating score was significantly lower in the dexmedetomidine group when compared with group B. They concluded that the use of dexmedetomidine via epidural route during one lung ventilation significantly decreases the anaesthetic requirement preventing awareness during anaesthesia and improving intraoperative oxygenation and postoperative analgesia.

3. S.V. Mohan et al[3] studied the effect of thoracic epidural infusion for post thoracotomy pain by comparing fentanyl-bupivacaine mixture with fentanyl alone. The study was conducted on 106 patients who were scheduled to undergo pulmonary resection. Patients were allocated to three different groups namely group F, FB1 and FB2. The group FB1 received infusion containing fentanyl 10µg/ml with

bupivacaine 0.1% and group FB2 received infusion containing fentanyl10µg/ml and bupivacaine 0.2% while the patients in group F received infusion of fentanyl10µg/ml alone . They found no inter - group differences in OVRS (observer/ verbal ranking scale for pain) at any time. At 2 hours they found that the visual analogue scores while coughing were significantly higher in group F than group FB1 or FB2. Otherwise they found no differences in pain scores or in the total amounts of epidural solution used. There were no complaints of motor or sensory abnormalities by any patients in both the groups. The number of patients who received interventions for hypotension included 3 patients in groups F, 5 and 7 patients in group FB1 and FB2 respectively. The requirement for vasopressor was higher in the FB2 group. The number of patients who complained of nausea included 15, 9 and 12 respectively in groups F, FB1 and FB2 respectively. The number of patients who complained of pruritus included 13, 15 and 14 in groups F, FB1 and FB2 respectively. They concluded that in the early postoperative period 0.1% bupivacaine provides better analgesia with fentanyl in patients undergoing lung

resection and is not associated with any disadvantages seen with bupivacaine 0.2%.

4. Jain D et al[4] studied the effect of epidural dexmedetomidine with intrathecal bupivacaine on hemodynamic parameters and quality of analgesia in the perioperative period in patients undergoing elective lower limb orthopaedic surgery. In this study 60 male patients between 20 – 50 years of ASA status 1 and 2 were recruited. They were randomly allocated to two groups. Group 1 received 2.5ml of 0.5%bupivacaine intrathecallly plus 10ml of normal saline epidurally whereas group 2 received the same intrathecal bupivacaine dose with dexmedetomidine 2µg/kg made up to 10ml epidurally. The results showed that the patients receiving epidural dexmedetomidine had a prolonged duration of analgesia of 424.1minutes when compared to the control group (140.0min). A significant fall in the pulse rate and mean arterial pressure was noticed in group 2 patients at all intervals until the end of the period of study. However both heart rate and blood pressure remained within the physiological range at all time intervals in the

dexmedetomidine group. Sedation score was between 3 and 4 in majority of the patients after 10-15min after administration of dexmedetomidine and lasted for 45±5 min. They concluded that addition of dexmedetomidine prolongs the duration of analgesia, decreases the requirement of rescue analgesics with significant fall in pulse rate and mean arterial pressure in patients undergoing elective lower limb orthopaedic surgery.

5. Ashraf Amin et al[5] studied the analgesic efficacy of dexmedetomidine in patients undergoing major abdominal cancer surgery. Ninety patients were randomized into 3 groups to receive either 10mg bupivacaine 0.5% intrathecally (control group n=30), or 10mg bupivacaine 0.5% with dexmedetomidine 5µg (dexmedetomidine group n=30), or 10mg bupivacaine 0.5% with dexmedetomidine 5µg and fentanyl 25µg (dexmedetomidine + fentanyl group n= 30). The patients were assessed for parameters like pain severity, first analgesic request time, total consumption of analgesics , hemodynamics, sedation score and side effects during the first 24 hours. They noticed that the mean intraoperative heart rate was significantly lower in the

group of patients receiving dexmedetomidine when compared with the control group. Though there was a significant reduction in the mean intraoperative systolic and diastolic pressure in the patients receiving dexmedetomidine there was no difference between the groups on postoperative hemodynamics or sedation score. The mean VAS values were significantly lower immediately and at 12 hours in both group of patients receiving dexmedetomidine compared to the control group. The mean time of the first analgesic request was significantly prolonged in the dexmedetomidine group (3.30±0.87 hours) and the dexmedetomidine+fentanyl group (5.41±1.23 hours) compared with the control group (0.23±0.11hours). They also recorded that the postoperative tramadol consumption was significantly less in the dexmedetomidine group when compared to the control group. They found significant differences in pruritus and vomiting among groups whereas no difference was noted to the incidence of nausea among groups. They concluded that providing dexmedetomidine intrathecally significantly improved the quality and duration of analgesia with analgesic sparing effect in patients undergoing major abdominal cancer surgery.

6. Saadawy et al[6] studied the effect of dexmedetomidine on the caudal block characteristics of bupivacaine in pediatric patients. Sixty children of ASA grade 1 aged between 1 to 6 years undergoing unilateral inguinal hernia repair /orchidopexy were recruited for the study. They were randomly allocated to two groups with 30 children in each group. Group B received a caudal injection of bupivacaine 0.25%, 1ml/kg; whereas the group BD received the same dose of bupivacaine mixed with dexmedetomidine 1µg/kg during sevoflurane anaesthesia. The parameters recorded included heart rate, blood pressure, pulse oximetry, end-tidal sevoflurane and bispectral index score every 5 minutes. Postoperatively the parameters recorded included emergence characteristics, pain and sedation score and quality of sleep. Duration of analgesia and requirement for additional analgesics was noted. It was found that the anaesthetic requirements in terms of end tidal sevoflurane concentration required to maintain target BIS level was significantly lower in the BD group compared with the B group. It was also found that the incidence of agitation was significantly lower in the dexmedetomidine group. The time to first rescue analgesic dose was significantly longer in the

BD group (18.5±2.8h) when compared to the B group (6.2±2.8h). There was no significant hemodynamic instability in any of the patients during the postoperative period. The maximal decrease in heart rate was 38±8 beats/min in the dexmedetomidine group which occurred at mean times of 28±7 min. The mean duration of sedation was significantly prolonged in the dexmedetomidine group. They concluded that addition of dexmedetomidine to bupivacaine improved the caudal analgesia with fewer requirements for postoperative analgesics and with minimal respiratory and hemodynamic depression.

7. A.M.El-Hennawy et al[7] studied the effect of adding clonidine or dexmedetomidine to bupivacine for caudal analgesia in children. Sixty patients in the age groups of 6 months to 6 years were recruited for this study. The children received single caudal dose of bupivacaine 0.25% (1ml/kg) combined with either dexmedetomidine 2µ/kg in normal saline 1ml (Group A) or clonidine 2 µg/kg in normal saline 1 ml (Group B) or corresponding volume of normal saline (Group C) according to the group assigned after sevoflurane in oxygen anaesthesia. Postoperative analgesia,

rescue analgesia and side effects were assessed during the first 24 hour period. The postoperative analgesia time recorded a median of 5 hours compared with 16 and 12 hours in group A and B respectively. No clinically significant episodes of hypotension, bradycardia or respiratory depression were observed in the postoperative period. They concluded that addition of dexmedetomidine or clonidine to caudal bupivacaine in children undergoing elective lower abdominal surgeries significantly promoted analgesia. They also concluded that dexmedetomidine did not offer any advantage over clonidine with regard to the duration of analgesia in the postoperative period.

8. Hazem M. Fawzi et al[8] studied the effect of preemptive caudal dexmedetomidine –bupivacaine mixture following single level lumbar laminectomy in adult patients. The study was conducted in 50 adult ASA 1 and 2 patients undergoing elective single level lumbar hemipartial laminectomy. Group B (n=25) received caudal 20ml of isobaric bupivacaine 0.25% while group BD (n=25) received the same volume of isobaric bupivacaine with dexmedetomidine 1µg/kg. Hemodynamic changes, end tidal

sevoflurane, BIS, narcotic requirement intra and post operatively, PCA boluses, sedation score and time to first void were all recorded. It was found that there were no significant hemodynamic differences between the groups except for bradycardia in the group BD intra and postoperatively until 8 hours. The time to first rescue analgesia was longer in group BD (495.200±95.224) when compared to the group B (262.0±22.913). The other advantages of group BD included less fentanyl supplementation, lower BIS and less end tidal sevoflurane requirements intraoperatively. They concluded that dexmedetomidine supplementation lead to better analgesia, less analgesia supplementation together with lower intraoperative BIS.

9. Staffan Wahlander et al[9] studied the effect of intravenous dexmedetomidine as an adjunct to thoracic epidural analgesia with bupivacaine following thoracic surgery. They hypothesized that supplementation of low dose thoracic epidural bupivacaine infusion by intravenous dexmedetomidine will lower the analgesic requirement without causing any respiratory depression. Twenty eight

patients who were scheduled to undergo elective thoracotomy for lobectomy or pneumonectomy were recruited for the study. The patients were loaded with bupivacaine 0.125% to T4 sensory level followed by a continuous infusion of 0.125% bupivacaine without opioid at 4ml/hour. The patients were then randomized into two groups. The dexmedetomidine group received a continuous i.v. infusion of 0.4µg/kg/hour following a bolus dose of 0.5µg/kg over 20 minutes. The analgesic requirement was measured by VAS and PCEA dosing and other additional analgesic use was recorded. They found no significant difference between the groups in terms of VAS score and PCEA use. They noticed that the requirement for supplemental fentanyl was greater in the placebo group. The patients belonging to the dexmedetomidine group also had decreased heart rate and blood pressure when compared to the placebo group. They concluded that i.v. dexmedetomidine can be used as an effective analgesic adjunct to thoracic epidural bupivacaine infusion which can decrease the opioid requirement and the potential for respiratory depression.

10. Mario Concha et al[10] compared epidural fentanyl/bupivacaine with intercostal nerve block with intravenous morphine for analgesia after thoracotomy. They compared the quality of analgesia and lung function in two groups of patients undergoing posterolateral thoracotomy. The patients in group 1 (n=16) received a 5 segment intercostal block plus i.v. PCA morphine and group 2 patients (n=15) received fentanyl and bupivacaine infusion for analgesia. They found that the patients in group 2 had lower resting and dynamic scores but only the resting scores were statistically significant. They showed that since the difference in pain scores is not clinically significant intercostal blockade with bupivacaine plus i.v. morphine PCA is a good alternative for post thoracotomy pain management.

11. Arjunan Ganesh et al[11] studied the efficacy of adding fentanyl to bupivacaine epidural infusion for postoperative analgesia in infants undergoing thoracotomy for lung resection. They recruited 32 infants randomly to receive either 0.1% bupivacaine infusion (group B, n=16) or 0.1% bupivacaine with 2µg/ml fentanyl (group BF, n=16).

Patients were evaluated for a period of 24 hours for pain, time to first rescue analgesia and complications. The rescue doses were given by intravenous nalbuphine. They noticed that the pain scores and nalbuphine consumption were significantly decreased in the group BF compared to group B. The time to first rescue analgesia was significantly longer in the group BF (516±524min) than in group B (126±89min). They noticed that incidence of side effects and the time to discharge and the time to first successful feeding were similar in both the groups.

12. M. Licker et al[12] studied the influence of thoracic epidural analgesia on the autonomic control of cardiovascular functions after thoracic surgery. They divided thirty eight patients into two groups to receive either patient controlled analgesia (PCA) or thoracic epidural analgesia (TEA) with bupivacaine (0.25% during operation, 0.125% after operation) and fentanyl (2µg/ml). The cardiovascular autonomic functions were assessed by heart rate variability, baroreflex function and pressure response to nitroglycerine and phenylephrine. They were assessed before surgery and 4 hours after the surgery and

during the first and second postoperative days. They concluded that using low concentrations of bupivacaine and fentanyl blunted cardiac symphathetic neural drive resulting in vagal predominance and better restoration of heart rate variables when compared with PCA management.

13. Constant et al[13] studied the effect of adding clonidine or fentanyl to local anaesthetic on the duration of surgical analgesia in children undergoing single shot caudal block. They recruited 64 children between the age group 6 to 108 months undergoing bilateral correction of vesicoureteral reflux lasting more than 90 minutes. The children were allocated into four groups. Group O received bupivacaine (0.25%) with epinephrine and lidocaine (1%) in equal parts. Group F received the same mixture of local anaesthetics with fentanyl 1µg/kg, group C received the same mixture of local anaesthetics with clonidine 1.5µg/kg and group C+F received local anaesthetics with fentanyl 0.5µg/kg and clonidine 0.75µg/kg. It was found that the single shot of epidural was sufficient only in 57% of the children in group O compared with 93% in group C and F and 86% in group C+F. The time to the first administration of analgesic was

significantly longer in the three groups of children who received additives but there were not any differences among the groups who received additives. Vomiting was noticed in the fentanyl group and the clonidine group had added advantage as it did not produce clinically significant side effects.

14. Sukhminder et al[14] did a comparative evaluation of clonidine and dexmedetomidine in epidural anaesthesia. They recruited 50 female patients of ASA 1 and 2 in the age group of 44 and 65 years who underwent vaginal hysterectomies. The patients were allocated to two treatment groups RC (Ropivacaine and clonidine) and RD (Ropivacaine and dexmedetomidine) with 25 patients in each groups. Group RC was administered 17ml of 0.75% epidural ropivacaine and 2µg/kg of clonidine and group RD was administered 17ml of 0.75% ropivacaine and 1.5µg/kg of dexmedetomidine. The parameters assessed included onset of analgesia, sensory and motor block levels, sedation, duration of analgesia and side effects. They noticed earlier onset of sensory analgesia and modified bromage scale 3 with dexmedetomidne when compared to

clonidine. The sedation scores were also significantly higher in the dexmedetomidine group. The time to rescue analgesia was longer in the dexmedetomidine group (342.88±29.16) when compared to the clonidine group (310.76±23.76). The sedation scores were significantly better in the dexmedetomidine group. They noticed a little higher incidence of dry mouth and nausea in both the groups. They concluded that dexmedtomidine is a better neuraxial adjuvant as it provided early onset of analgesia, adequate analgesia and prolonged post- operative analgesia.

15. Vijay G Anand et al[15] conducted a randomized double blinded study to compare the effects of caudal dexmedetomidine when added to ropivacaine in 60 children undergoing lower abdominal surgeries. They were divided into group RD (n=30) who received 0.25% ropivacaine 1ml/kg with dexmedetomidine 2µg/kg and group R who received 0.25% ropivacaine 1ml/kg with normal saline. The duration of postoperative analgesia was a median of 5.5 hours in group R compared to 14.5 hours in group RD. They concluded that caudal dexmedetomidine (2µg/kg) with 0.25% ropivacaine (1ml/kg) in paediatric lower abdominal

surgeries resulted in significant postoperative pain relief that resulted in a better quality of sleep and a prolonged duration of arousable sedation and produced less incidence of emergence agitation following sevoflurane anaesthesia.

MATERIALS AND METHODS

The present study was conducted after obtaining institutional ethical approval on adult patients admitted to Rajiv Gandhi Govt. General Hospital. The recommendations guiding medical doctors in biomedical research involving human subjects contained in the “eighteenth declaration of Helsinki” adopted by the world medical assembly, Helsinki, Finland, 1964 were adhered to throughout the study.

INCLUSION CRITERIA:

Adult patients aged 18 – 60 years undergoing elective thoracotomy with ASA physical status II & III who have given valid informed consent.

EXCLUSION CRITERIA:

- Patients younger than 18 years or older than 60 years.
- Known allergy to bupivacaine or anaesthetic drugs.
- Patients with deformities of vertebral column.
- Patients with hepatic or renal insufficiencies.
- Patients with neurological or psychiatric illness.

- Patients with coagulation disorders.
- Patients with BMI > 35 Kg/$m^{2.}$
- Patients with pre existing motor or sensory deficits.
- Patients with predicted post operative fev1 < 40 %

Written consent was obtained from all the patients after explaining the procedure. For all patients age, weight and height were noted. In the assessment room, vital parameters like pulse rate, blood pressure and baseline investigations like hemoglobin, blood sugar, urea and creatinine, CXR and ECG were checked. Pulmonary function tests were done preoperatively in all patients. Thorough examination of all the systems and airway examination were done. Visual Analogue Scale (VAS) was explained to the patients. The patients were shown a 10 cm long scale marked from 0 – 10 on a blank paper and told that 0 represented “no pain” and 10 represented “worst possible pain”.

MATERIALS USED:

1. 16 G, 9 cm Touhy needle, with Hueber’s tip,
2. 18 G epidural catheter, filter,

3. Loss Of Resistance syringe,
4. 5 ml syringe,
5. local anaesthetic preparation of 1.5 % lignocaine with 1 in 2 lac adrenaline,
6. Sterile drapes,
7. Visual analogue scale

DRUGS USED:

- Bupivacaine
- Fentanyl
- Dexmedetomidine

PARAMETERS STUDIED:

Primary outcome measures:

- **Duration of analgesia**: The time interval from injection of epidural drug to rescue analgesia.
- **Quality of analgesia** as assessed by visual analogue score.
- **Level of Sedation** as assessed by a five point sedation scale.

Secondary outcome measures:

- **Hemodynamic parameters** – variations in heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial blood pressure.
- **Side effects** – respiratory depression, pruritus, nausea and vomiting, dry mouth, if any.

BRIEF PROCEDURE:

Fifty adult patients (18 – 60 years) undergoing elective thoracotomy and planned for epidural analgesia post operatively were included in this randomized double blinded study. They were randomly allocated to two groups; group D and group F. Group allocation was done by closed envelope method.

GROUP D: Received 8ml of 0.125% bupivacaine and 1µ/kg of dexmedetomidine diluted to 2ml via the epidural catheter.

GROUP F: Received 8ml of 0.125% bupivacaine and 1µ/kg of fentanyl diluted to 2ml via epidural catheter.

The total volume of local anaesthetic solution administered to all the patients was 10 ml. The solutions were prepared by an anaesthetist not involved in the study and the postoperative observer was blinded to the group allocation of the patient.

On the day of surgery in the operating room, basic monitors like ECG, pulse oximeter and non invasive blood pressure were connected and a peripheral i.v. access was obtained using a 16 G i.v. canula. Patients were premedicated with midazolam 0.02mg/kg i.v., inj.ranitidine 50mg i.v., and inj. Glycopyrrolate 0.2mg i.v. and hydrated with 500ml of Ringer's Lactate solution. Patients were put in the right lateral position, the back was cleaned with povidone iodine solution and draped with sterile towels. 2 – 3 ml of 2% lignocaine was infiltrated subcutaneously and 16 G tuohy epidural needle was introduced into the T_{6-7} or T_{7-8} interspinous space. In all patients the midline approach was used to enter into the interspinous space. Epidural space was identified using loss of resistance to air. Epidural catheter was inserted and directed in the cephalic direction, 3cm into the epidural space. The catheter

insertion site was tightly secured on the back with plasters and a bacterial filter was attached to the epidural catheter. If vascular puncture was encountered, the space above was chosen for the block. If dural puncture was encountered during the attempt, the space above the one which had dural puncture was used to give the block. After successful catheterisation the patients were turned supine and a 3 ml test dose of 1.5% lignocaine with 1in 2,00,000 adrenaline was given through the epidural catheter to rule out intrathecal or intravascular placement. The patients were preoxygenated for 3 – 5 min. Inj. Fentanyl 2µg/kg was used as analgesic. Patients were induced with inj. thiopentone 5mg/kg. Inj.vecuronium 0.1mg/kg was given for neuromuscular blockade followed by intubation with appropriate sized single lumen or double lumen endotracheal tube, according to the case. Correct tube position was confirmed by auscultation. In all patients bladder was catheterised prior to surgery. Anaesthesia was maintained with sevoflurane with oxygen 40% and nitrous oxide 60% and vecuronium. Intraoperatively analgesia was provided by fentanyl and repeated regularly as required. Blood loss was replaced and other complications were

managed appropriately. All the patients were given diclofenac 100mg suppository at the end of surgery to attenuate any anticipated visceral or shoulder tip pain in the post operative period. After the surgery was over, patient's blood pressure and heart rate were noted down. These values were taken as the baseline values for the subsequent hemodynamic measurements. The study drug was administered at the end of the surgery via the epidural catheter, after carefully aspirating the syringe for the presence of blood or csf. The drug was injected at a rate of 1ml per second. Once the patients had spontaneous respiratory attempts they were reversed with 50 µ/kg neostigmine and 20 µ/kg of glycopyrolate. Patients were extubated after adequate recovery of pharyngeal reflexes. Visual analogue scoring and vital parameters were recorded 15 minutes after giving the study drug or after extubation, whichever was later.

Procedure was considered as a failure if, there was unsatisfactory post operative analgesia with a VAS greater than 4 at the first assessment at 15 minutes after giving the block or after extubation, whichever is later.

POST OPERATIVE MONITORING:

Patient's vital parameters – HR, SBP, DBP, MAP, RR, SpO_2, level of sedation and pain assessment were done every 15 min in the first hour, every half an hour in the second hour and then hourly for 6 hours. Pain assessment was done using visual analogue score as marked by the patients and sedation was assessed by the five point sedation score. In all the patients supplementary oxygen was given via a facemask with flow of 3 – 4 litres per minute for 12hours.

GRADING OF VISUAL ANALOGUE SCORE:

0 – Does not hurt.

2 – Hurts just a little bit.

4 – Hurts a little more.

6 – Hurts even more.

8 – Hurts a lot.

10 – Hurts as much as you can imagine.

FIVE POINT SEDATION SCORE:

Grade 1 - alert, awake, no sedation

Grade 2 - arousable to verbal command

Grade 3 - arousable with gentle tactile stimulation

Grade 4 - arousable with vigorous shaking

Grade 5 - unarousable

At any point of time when the VAS was more than 3, rescue analgesia was given. The time interval between the administration of epidural drug and the first analgesic dose was calculated as the duration of analgesia. Rescue analgesia was given in the form of intravenous morphine up to a maximum of 0.2 mg /kg.

Any episode of sedation, nausea, vomiting, itching, motor blockade, hypotension, bradycardia and low respiratory rate were recorded at the same time as pain scores.

SIDE EFFECTS:

Bradycardia was defined as a heart rate slower than 50 beats per minute for the purpose of this study. It was treated with inj. Atropine 0.6mg i.v.

Hypotension was defined as systolic blood pressure less than 90 mmhg or a fall in mean arterial pressure more than 20% from baseline and was treated with a rapid infusion of 250 ml of normal saline. This was followed by inj. Ephedrine 3mg i.v. in repeated boluses, if the systolic blood pressure did not increase above 90mmhg within 2 minutes from the baseline value.

Respiratory depression was defined as respiratory rate below 8 per minute. It was managed with supplementary oxygen. Hypoxia was defined as a saturation of less than 90 % and was managed with supplementary oxygen. Vomiting was managed with inj. Ondansetron 4 mg i.v.

OBSERVATION AND RESULTS

We enrolled a total of 50 patients who underwent elective thoracotomy in the study and randomly divided them into two groups. 25 patients were allotted to group D and 25 were allotted to group F.

Calculation of sample size:

The sample size was calculated using openepi software version 2.3. Sample size was calculated with an alpha error of 5%, power of 95% and mean time required for first analgesic requirement in dexmedetomidine group of 366 minutes with a standard deviation of 24.42[(1)]. We assumed a decrease in value of 5% to be clinically significant. Using these values the sample size was 24 in each group. Hence we recruited 25 subjects in each group.

Results have been expressed as mean with standard deviation for duration of analgesia, quality of analgesia, heart rate and blood pressure variations. Level of sedation was expressed as median with range. Side effects have been expressed as number and percentage. All statistical

analysis was done using SPSS for windows version 15.0. We used t – test for comparing quantitative variables and chi – square test for comparing qualitative variables. A p value of less than 0.05 was considered statistically significant.

DEMOGRAPHIC DATA:

Table No. 1: Demographic Profile (student's *t* test)

Demographic Characteristics	Group D Mean ± S.D.	Group F Mean ± S.D	P value
Age (years)	36.68±8.24	40.72±6.55	0.338
Weight (kg)	61.72±7.76	63.60±7.43	0.386
Height (cm)	165±4.66	166±4.26	0.530
BMI (kg/m^2)	22.33±1.89	22.95±1.68	0.229
Sex Ratio (M:F)*	64:36*	72:28*	0.544
ASA (II:III)*	60:40*	56:44*	0.774
Duration of surgery (min)	182±9.41	181±10.38	0.854
Type of surgery*			0.787
- Lobectomy	15	15	
- Mass excision	1	1	
- Bulla excision	1	0	
- Decortication	8	9	

* (chi-square test)

Both the groups were comparable in their demographic characteristics like age, height, and weight and body mass index. The mean age of patients allotted in group D was 36.68 yrs and was 40.72 yrs in patients allotted to group F. The age distribution in group D was from 25 to 55 yrs and in group F was from 28 to 57 yrs. The mean body mass index of the patients was 22.33 in group D and 22.95 in group F.

There were 16 male patients in group D and 18 male patients in group F. There were 9 female patients in group D and 7 female patients in group F. The sex ratio was similar in both the groups.

The distribution of patients according to ASA physical status were similar in both the groups: 15 patients in the dexmedetomidine group and 14 patients in fentanyl group belonged to ASA class II. 10 patients in the dexmedetomidine group and 11 patients in fentanyl group belonged to ASA class III.

The types of surgery performed were also equally distributed between the two groups. 15 patients in each of the two groups had undergone lobectomies, 8 patients in group D and 9 patients in group F had undergone decortications, 1 patient each in both the groups had undergone lung mass resection and 1 patient in group D had a bulla excision.

The mean duration of the surgery was 182 minutes in group D and 181 minutes in group F, being similar in both. All the patients who were enrolled in the study were extubated on table after surgery. Intercostal drainage tubes were inserted in all the patients at conclusion of surgery. No resection of ribs was done in any of the patients. In two patients attempted epidural catheterisation was unsuccessful and they were excluded from the study. Three patients had excessive blood loss during surgery and major fluid shifts and they were excluded from the study. Accidental dural puncture during epidural catheterisation occurred in three patients but there was no incidence of post dural puncture headache in any of them.

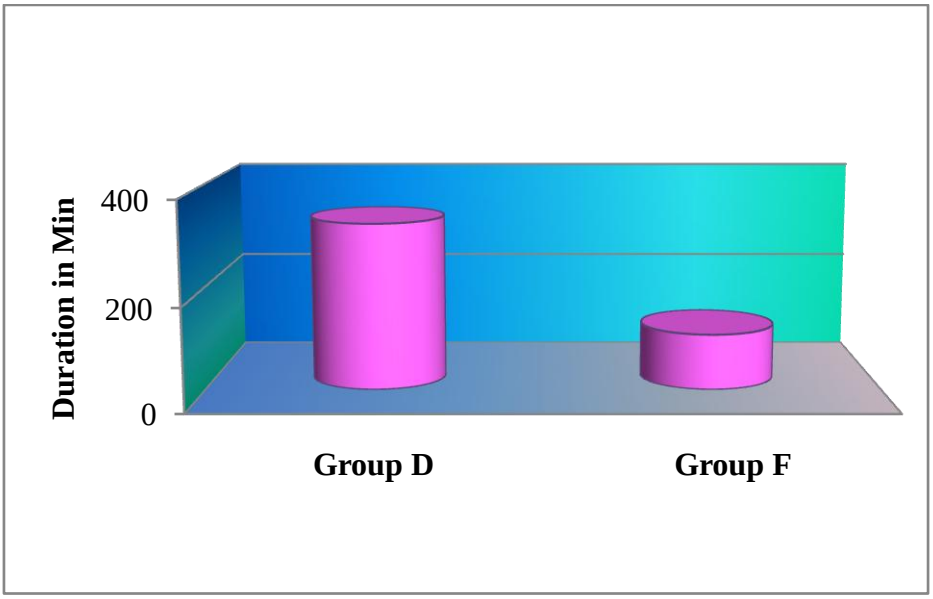
DURATION OF ANALGESIA:

With respect to the pain relief, patients in the D (dexmedetomidine) group had a smooth and prolonged post operative analgesia when compared to F (fentanyl) group. The mean duration of analgesia as determined by the time to first rescue analgesia was significantly longer in the dexmedetomidine group (329.92 ± 23.058min) when compared to the fentanyl group (110 ± 9.345 min) with a p value of <0.001 which was statistically highly significant.

Table No.2: Comparison of mean duration of analgesia (student's *t* test)

Group	Mean Duration Of Analgesia (Minutes)	Standard Deviation	P value
D	329.92	23.058	<0.001
F	110	9.345	

Bar Diagram No.1: Comparison of Duration of Analgesia



QUALITY OF ANALGESIA:

Table No. 3: Comparison of Postoperative Visual Analogue Scores (student's *t* test)

Time In Minutes	Group D Mean ± S.D.	Group F Mean ± S.D.	P Value
30	0.00 ± 0.00	1.12 ± 0.66	<0.001
45	0.04 ± 0.20	1.20 ± 0.64	<0.001
60	0.32 ± 0.47	2.00 ± 0.40	<0.001
90	0.60 ± 0.50	2.40 ± 0.50	<0.001
120	1.24 ± 0.59	3.76 ± 0.43	<0.001
180	1.76 ± 0.52	-	-
240	2.32 ± 0.47	-	-
300	3.16 ± 0.55	-	-
360	3.92 ± 0.27	-	-

The patients in the D group experienced less pain than the F group. Visual analogue scores were always below 3 in both the D and F group and were much lower in the D group when compared to the F group. The mean visual analogue score during the period of analgesia was 1.25±0.25 in patients belonging to group D and 1.68±0.31 in patients belonging to group F which was highly significant (p value <0.001). Visual analogue scores in the dexmedetomidine group were 0 in the first one and a half hours and were between 1-2 in the next two hours and 3 thereafter. In the fentanyl group the visual analogue score was between 1 and 3 in the 2 hour period. The differences in VAS between the two groups at all the time intervals were statistically highly significant.

LEVEL OF SEDATION:

The sedation scores for both the groups are expressed as median and range. Median sedation scores were significantly higher in the dexmedetomidine group compared to the fentanyl group. The patients were calm, easily arousable and comfortable in the dexmedetomidine group. The median sedation scores were between 2 and 3 in

the first two and a half hours & between 1 and 2 in the next three hours in the dexmedetomidine group. In the fentanyl group the median sedation scores were ranging from 1 to 2.

Table No.4: Comparison of Sedation Scores (Chi-Square test)

Time Min	Group D Median(Range)	Group F Median(Range)	P Value
15	3(2-3)	2(1-2)	<0.001
30	3(2-3)	1(1-2)	<0.001
45	3(2-3)	1(1-2)	<0.001
60	3(2-3)	1(1-2)	<0.001
90	2(2-3)	1(1-2)	<0.001
120	2(2-3)	1(1-2)	<0.001
180	2(1-3)	-	-
240	1(1-2)	-	-
300	1(1-2)	-	-
360	1(1-2)	-	-

No patients in either of the groups had sedation score of 4 or 5 at any point of time. The percentage wise distribution of sedation scores at various time intervals

between the two groups are summarised in the following table.

Table No.5: Distribution of Sedation Scores between the Two Groups

Time in minutes	Sedation score 1		Sedation score 2		Sedation score 3	
	Group D No. of pts (%)	Group F No. of pts (%)	Group D No. of pts (%)	Group F No. of pts (%)	Group D No. of pts (%)	Group F No. of pts (%)
15	0 (0%)	2 (8%)	1 (4%)	23 (92%)	24 (96%)	0 (0%)
30	0 (0%)	20 (80%)	4 (6%)	5 (20%)	21 (89%)	0 (0%)
45	0 (0%)	21 (84%)	4 (16%)	4 (16%)	21 (84%)	0 (0%)
60	0 (0%)	25(100%)	10 (40%)	0 (0%)	15 (60%)	0 (0%)
90	0 (0%)	25 100%)	12 (48%)	0 (0%)	11 (44%)	0 (0%)
120	0 (0%)	25(100%)	25(100%)	0 (0%)	0 (0%)	0 (0%)
180	2 (8%)	-	22 (88%)	-	1 (4%)	-
240	14 (56%)	-	11 (44%)	-	0 (0%)	-
300	23 (92%)	-	2 (8%)	-	0 (0%)	-
360	24 (96%)	-	2 (8%)	-	0 (0%)	-

HEMODYNAMIC CHANGES:

Systolic Blood Pressure:

There was a fall in systolic blood pressure from the baseline after injection of the drug in both the groups. The decrease in blood pressure was mild and gradual in both the groups. There was no statistically significant between the two groups in the first 45 minutes after injection on drug. In the 60 to 120 minute period the systolic blood pressure values of group D was lesser than group F and was statistically significant. After two hours, there was a steady rise in systolic blood pressure in group D almost approaching baseline values and was stable.

Line diagram No.1: Comparison of systolic blood pressures

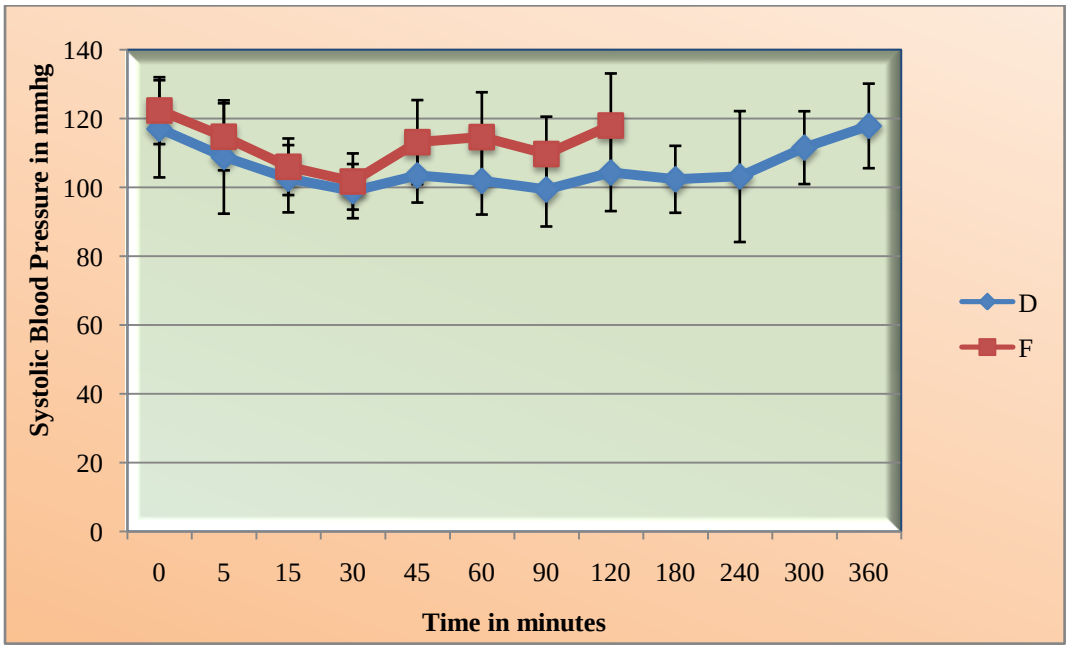


Table No.6: Comparison of systolic blood pressure (student's *t* test)

Time minutes	Group D Mean ± S.D.	Group F Mean ± S.D.	P value
0	117.08±14.12	122.36±9.725	0.130
5	108.88±16.47	114.76±9.748	0.131
15	102.56±9.78	106.04±8.228	0.180
30	98.96±7.87	101.76±8.171	0.223
45	103.56±7.92	113.20±12.23	0.002
60	101.96±9.81	114.6413.073	0.000
90	99.44±10.76	109.7210.888	0.002
120	104.36±11.20	118.00±15.17	0.001
180	102.40±9.73	-	-
240	103.20±19.03	-	-
300	111.60±10.59	-	-
360	117.92±12.29	-	-

Diastolic Blood Pressure:

Similar to the systolic blood pressures, there was a mild and gradual fall in diastolic blood pressures after injection of drug in both the groups. There were no statistically significant differences in diastolic blood

pressures between the two groups in the first 60 minutes of injection of drug. At 90 minutes and at 120 minutes the diastolic blood pressure values of group D was lesser than group F and was statistically significant. After two hours, there was a steady rise in systolic blood pressure in group D almost approaching baseline values and was stable.

Line Diagram No.2: Comparison of Diastolic Blood Pressures

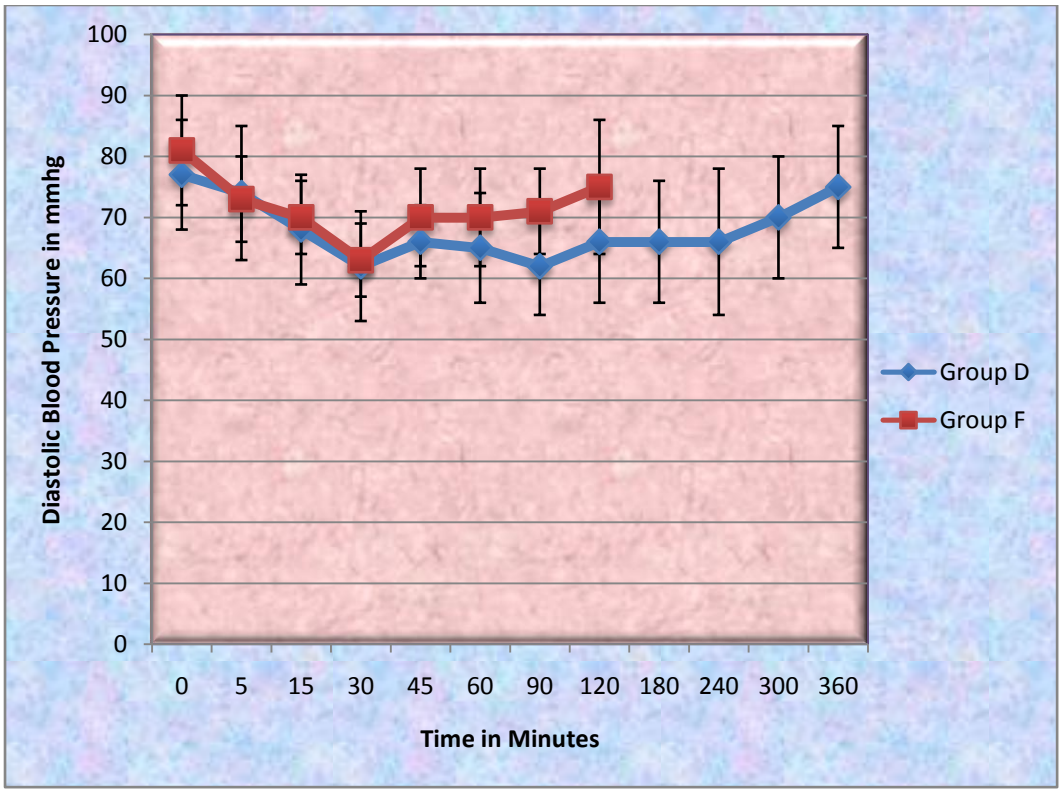


Table No.7: Comparison of diastolic blood pressure

Time minutes	Group D Mean ± S.D.	Group D Mean ± S.D.	P value
0	77.32±9.72	81.529.097	0.121
5	74.32±11.88	73.12±7.93	0.676
15	68.96±9.58	70.48±6.79	0.521
30	62.60±9.44	63.88±6.68	0.583
45	66.96±6.61	70.52±8.12	0.096
60	65.92±9.88	70.56±8.37	0.080
90	62.72±8.58	71.84±7.65	0.001
120	66.80±10.73	75.64±11.547	0.007
180	66.12±10.89	-	-
240	68.80±12.28	-	-
300	70.44±10.39	-	-
360	75.76±10.60	-	-

Mean Arterial Pressure:

There was a 10 to 15% decrease in the mean arterial pressure in both the groups after injection of the drug; corresponding to the systolic and diastolic blood pressure values. The differences between the mean arterial pressures were similar during the first 45 minutes of injection of the

drug. After 45 minutes, up to two hours, the mean arterial pressures were significantly lesser in the dexmedetomidine group than in the fentanyl group. Later there was a steady increase in mean arterial pressure approaching towards the baseline values in group D. The absolute values are depicted in table no. 8.

Table No.8: Comparison of Mean Arterial Pressure

Time in minutes	Group D mean ± S.D	Group F Mean ± S.D.	P value
0	89.00±12.148	95.00±9.083	0.054
5	85.12±11.76	85.76±8.861	0.829
15	79.84±8.11	83.72±6.937	0.075
30	72.48±6.92	75.48±7.136	0.138
45	79.32±6.34	83.80±9.055	0.048
60	77.76±8.30	84.32±9.890	0.014
90	74.96±9.11	84.64±8.631	0.001
120	78.96±8.87	89.44±12.292	0.001
180	78.84±7.79	-	-
240	80.84±10.94	-	-
300	84.44±9.31	-	-
360	88.96±10.46	-	-

Line Diagram No.3: Comparison of Mean Arterial Pressures

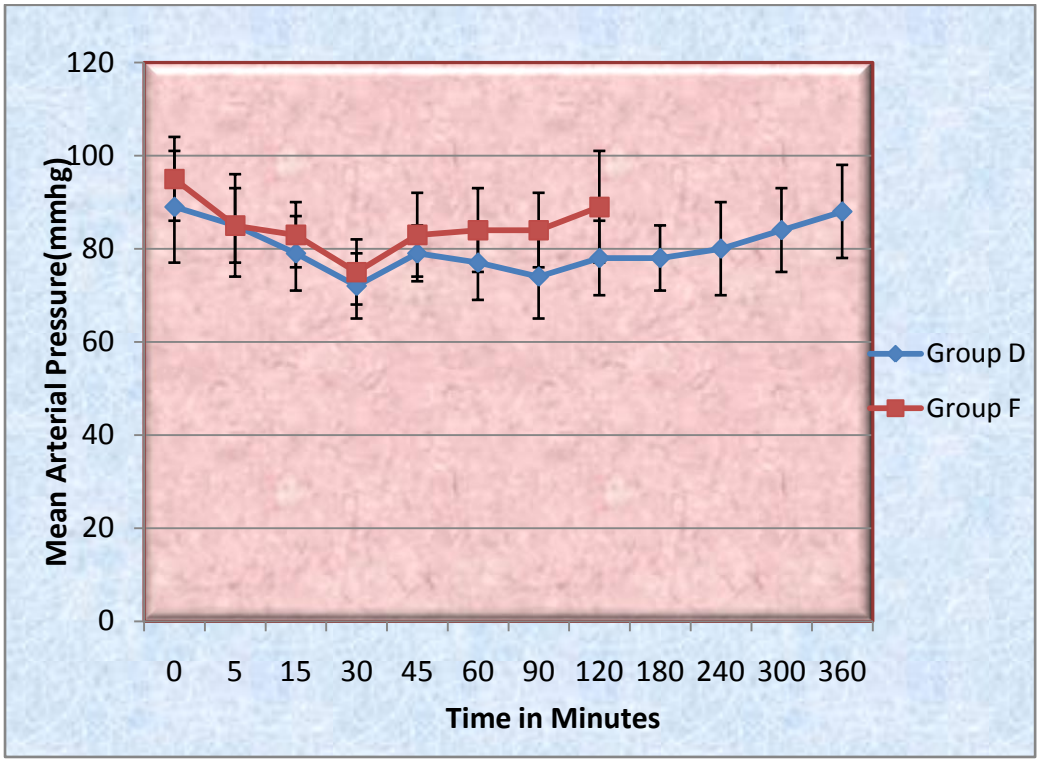


Table No.9: Comparison of Decrease in Mean Arterial Pressure

MAP	Group D Mean ± S.D.	Group F Mean ± S.D.	P value
Baseline(mmhg)	89.00 ± 12.14	95.00 ± 9.08	0.054
Maximal Decrease(mmhg)	17.72 ± 9.05	20.92 ± 10.17	0.246
Percentage of Maximal Decrease	19.91% *	22.02%*	
Time (min)	33.00 ± 6.124	31.20 ± 7.39	

*percentage

The magnitude of maximal decrease in the MAP was 17mmhg in the D group and 20.92mmhg in F group as shown in table no.9. The percentage of decrease in MAP was 19.91% in group D and 22% in group F. This decrease occurred at around 30 minutes of injection of drug in both the groups. The results were not statistically significant.

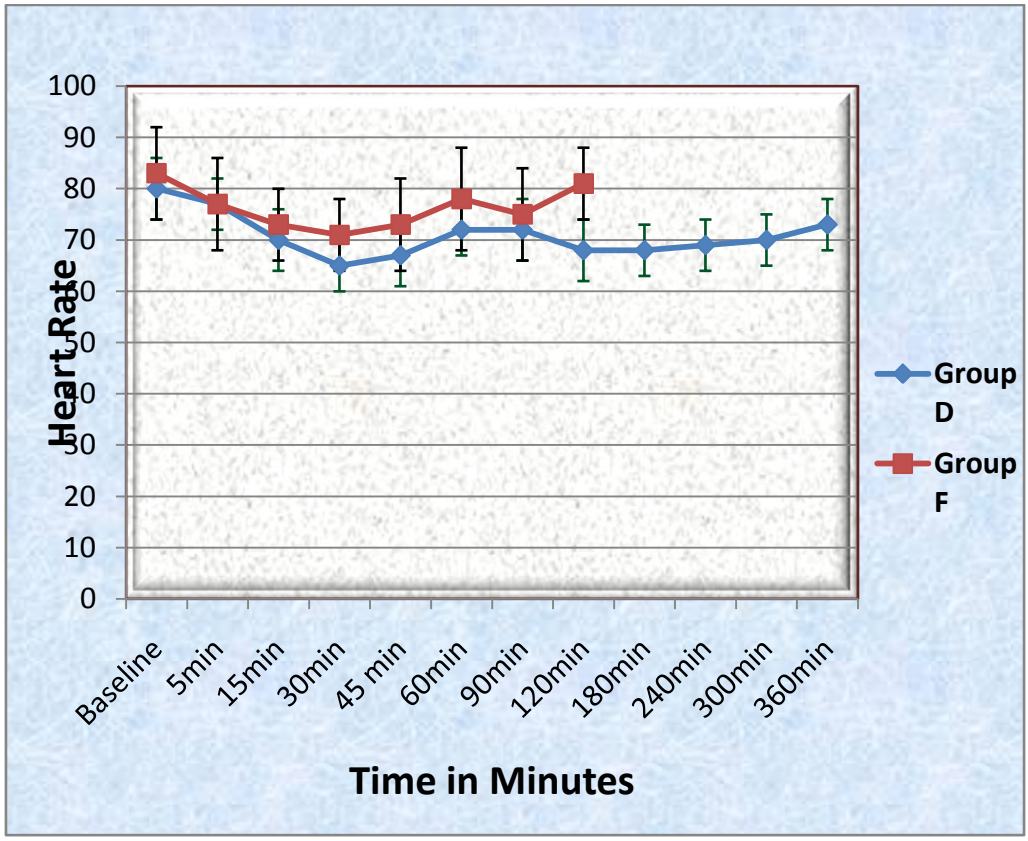
HEART RATE:

Heart rate reduction was observed in both the groups when compared to baseline values. But the amount of decrease was more in group D, being significant statistically in the second hour. After two hours there was a steady increase in heart rate, almost trying to approach baseline values.

Table No.10: Comparison of Heart Rate

Time in minutes	Group D Mean ± S.D.	Group F Mean ± S.D.	P value
0	80.32±6.26	83.48±9.06	0.158
5	77.48±5.83	77.52±9.97	0.986
15	70.36±6.42	73.48±7.55	0.122
30	65.19±5.63	71.68±7.38	<0.001
45	67.65±5.82	73.56±8.85	0.006
60	72.19±5.19	78.28±10.45	0.007
90	72.96±5.90	75.04±9.14	0.343
120	68.80±6.40	81.28±7.35	1.008
180	68.88±5.61	-	-
240	69.34±5.42	-	-
300	70.48±5.06	-	-
360	73.32±5.27	-	-

Line Diagram No.4: Comparison of Heart Rate



The magnitude of maximal decrease in heart rate was 16 beats per min in group D as compared to 12 beats per min in group F. The percentage of maximal decrease in the heart rate after injection of the drug was 19% in group D and 14% in group F. The peak time of decrease in heart rate was observed after 30 minutes of drug injection in both the groups. The percentage of maximum difference in heart rate was highly significant between the two groups with a p – value of 0.001.

Table No.11: Comparison of decrease in heart rate (student's *t* test)

Heart Rate	Group D Mean ± S.D.	Group F Mean ± S.D.	P value
Baseline HR	80.32±6.26	83.48±9.06	0.158
Magnitude of Maximal Decrease	15.84±2.83	11.80±5.18	0.001
Percentage of Maximal Decrease	19.39%*	14.13%*	
Time	28.20±6.5	29.20±9.4	

* percentage

SIDE EFFECTS:

There were no statistically significant differences between the groups in the incidence of nausea, vomiting, dry mouth and pruritus. The number and percentage of patients who complained of nausea, vomiting and dry mouth are summarized in the table.

Table No.12: Incidence of side effects (Chi-Square test)

Side Effect	Group D Number (%)	Group F Number (%)	P value
Bradycardia	1 (4%)	0 (0%)	0.312
Hypotension	1 (4%)	1 (4%)	1.000
Nausea	2 (8%)	3 (12%)	0.637
Vomiting	0 (0%)	2 (8%)	0.149
Dry Mouth	3 (12%)	0 (0%)	0.074
Pruritus	0 (0%)	2 (8%)	0.149
Respiratory Depression	0 (0%)	0 (0%)	1.000

There was one incidence of significant bradycardia in a patient in the D group. It was appropriately treated with atropine. There was no episode of bradycardia in the fentanyl group. Two patients – one in group D and one in group F had significant hypotension with no associated excessive blood loss. It subsided with intravenous fluids and ephedrine administration. There was no incidence of respiratory depression (RR < 10 or sPO_2 <90%) in either of the groups. There was no incidence of postoperative neurological deficit in any of the patients.

DISCUSSION

It is a well known fact that thoracic epidural analgesia provides effective pain relief after thoracotomy. The commonly used drugs for pain relief following thoracic epidural are usually local anaesthetics. When used in high concentration local anaesthetics are associated with hypotension. If given in low concentration the analgesia becomes often inadequate. Hence opioids were given as additives to local anaesthetic in order to decrease the need for administering high concentration of local anaesthetic. Epidural opioids did reduce the incidence of postoperative complications like atelectasis and pneumonia and were tried as a sole analgesic postoperatively but were not popular due to the higher concentration required and the due to the incidence of respiratory depression.

It is a well established fact that synergistic effect occurs when local anaesthetics and opioids are given together neuraxially. This can be used to reduce the concentration of local anaesthetics and opioids used by

epidural route for post operative analgesia and reduce the incidence of side effects when given separately.

Fentanyl is one of the commonly used neuraxial opioid along with local anaesthetics to provide better postoperative analgesia. But increasing the concentration of fentanyl to provide better postoperative analgesia is associated with dose dependent side effects like nausea, pruritus, sedation and respiratory depression.

In order to avoid the undesirable side effects of opioids like respiratory depression at high concentration especially after thoracotomy it may be desirable to use other neuraxial adjuvant like α2 adrenergic receptor agonists - clonidine and dexmedetomidine. Dexmedetomidine is more selective at α2 receptor when compared to clonidine. **Hence we used dexmedetomidine in this study.**

α2 adrenergic agonists (dexmedetomidine) also possesses analgesic properties like opioids but the advantage is that it lacks the respiratory depression like

opioids. Dexmedetomidine helps in maintaining sedation without cardiovascular instability or respiratory depression. Dexmedetomidine also acts synergistically with local anaesthetics by prolonging the duration of sensory and motor block and by providing prolonged duration of analgesia when compared to local anaesthetics alone.

In view of the advantages of dexmedetomidine we performed the study to compare the analgesic and adverse effect profile between epidurally administered fentanyl and dexmedetomidine in patients undergoing thoracotomy.

We found that dexmedetomidine is better when compared to fentanyl as it is superior in providing better pain score and more comfort and intense analgesia in the postoperative period. The duration of analgesia is more when dexmedetomidine is added to bupivacaine. The time to first rescue analgesia was approximately 320 minutes after the first dose whereas in case of fentanyl it is around 2 hours which is correlates with the study conducted by S Bajwa et al and Schnaider et al. No abnormal motor or sensory deficits were observed in any patients in both the

groups. Dexmedetomidine produces this effect of prolonged duration of analgesia by its action on the superficial dorsal horn of the spinal cord. It acts by inhibiting the release of neurotransmitters from primary afferent nerve terminals like substance P and glutamate and by causing hyperpolarisation of interspinal neurons.

Sedation score was higher in the dexmedetomidine group when compared to fentanyl group but none of the patients in either group had profound respiratory depression or deep sedation requiring intervention as mentioned in other studies. This could be due to the low dose of dexmedetomidine used in our study. The patients in the dexmedetomidine group were calm and awake and could communicate without any agitation. The sedation in the dexmedetomidine group is because of its action on the locus ceruleus causing decreased firing of the neurons along with inhibition of nor epinephrine release and activity in the descending medullospinal noradrenergic pathway, secondary to activation of central α2 adrenergic receptor. The reduced sedation score in the fentanyl group could be because of the lower dose of fentanyl used in our study.

Hemodynamic fluctuations were noticed in both the groups. The fall in the heart rate and blood pressure were noticed in both the groups but the fall was more in the dexmedetomidine group when compared to the fentanyl group. The maximum fall in heart rate and blood pressure was around 30 to 45 minutes in both the groups. Mean heart rate and blood pressure were stable in both the groups after this fall and none of them required any intervention after this. The patients were hemodynamically stable in both the groups. The maximum reduction of mean arterial pressure was around 19% in the dexmedetomidine group in our study, whereas Schnaeder et al and El Hennaway et al observed a 25% reduction in mean arterial pressure. This could be because they used 2 µ/kg of dexmedetomidine whereas in our study we used 1µ/kg. The fall in blood pressure and pulse rate caused by dexmedetomidine can be attributed to central α2A adrenergic receptor causing reduced release of nor adrenaline from the sympathetic nervous system.

There were complaints of pruritus by 2 patients in the fentanyl group while none of the patients in the

dexmedetomidine group complained of any pruritus. The pruritus occurred in both the patients within an hour after fentanyl administration and lasted for 30 minutes and was localized to the face. No intervention was required in both the patients as the symptoms resolved by its own.

Two patients in group D and 3 patients in Group F group complained of nausea. But none of the patients in either group required any intervention and was self limiting.

We did not notice any incidence of respiratory depression in both the groups. The reduced incidence of respiratory depression in the fentanyl group could be because of the low dose of the epidural fentanyl bolus given in these patients.

SUMMARY

This double blinded prospective randomized controlled study was done to evaluate the duration of analgesia as well as sedation and adverse effects of dexmedetomidine(1µg/kg) and fentanyl (1 µg/kg) given via epidural route with 0.125% bupivacaine in patients post operatively who underwent thoracotomy surgeries under general anaesthesia.

The following observations were made:

- The addition of dexmedetomidine to 0.125% bupivacaine significantly prolonged the duration of post operative analgesia compared to fentanyl.
- The quality of analgesia was significantly better when dexmedetomidine was added to bupivacaine rather than fentanyl.
- The addition of dexmedetomidine epidurally produced sedation that was arousable for many hours.

- The incidence of side effects such as hypotension, bradycardia, nausea, vomiting and pruritus were not statistically significant between the groups.
- No episode of respiratory depression was noted in both the study groups which are more common with opioids.
- Hemodynamic stability was well maintained in patients belonging to both the groups.

CONCLUSION

In conclusion, dexmedetomidine appears to have a beneficial effect as an adjuvant to local anaesthetic by improving the quality and increasing the duration of analgesia without the side effects associated with opioids like respiratory depression. It has minimal side effects and good hemodynamic stability. However its routine use in epidural route requires caution with regard to its effects due to central sympatholytic property and further studies are necessary to quantify the required dosage.

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INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI -3

Telephone No : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. M. Thiriloga Sundary
PG in MD Anaesthesia
Madras Medical College, Chennai -3

Dear Dr. M. Thiriloga Sundary

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "Prospective, randomized comparative study on the effect of adding dexmedetomidine and fentanyl to epidural bupi vacaine (0.125%) on post operative anlangesic in patients undergoing thoracotomy" No.39062012.

The following members of Ethics Committee were present in the meeting held on 19.06.2012 conducted at Madras Medical College, Chennai -3.

1. Dr. S.K. Rajan. M.D.,FRCP.,DSc -- Chairperson
2. Prof. K. Ramadevi MD -- Member
   Prof of Biochemistry, MMC, Ch-3
3. Prof. R. Nandhini MD -- Member
   Director, Inst. of Pharmacology ,MMC, Ch-3
4. Prof. C. Rajendiran, MD -- Member
   Director , Inst. of Internal Medicine, MMC, Ch-3
5. Prof. S. Deivanayagam MS -- Member
   Prof of Surgery, MMC, Ch-3
6. Prof. A. Radhakrishnan MD -- Member
   Prof of Internal Medicine, MMC, Ch-3

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

MASTER CHART

GROUP D – DEXMEDETOMIDINE											
S.NO	**NAME**	**AGE**	**SEX**	**WEIGHT**	**HEIGHT**	**BMI**	**ASA - PS**	**PROCEDURE**	**FAILURE**	**DURATION OF SURGERY (in minutes)**	**DURATION OF ANALGESIA (in minutes)**
1	Kathirvel	40	M	60	165	22.03	II	lobectomy	no	182	330
2	Muthusamy	45	M	65	170	22.49	III	decortication	no	170	350
3	Kuppan	50	M	66	169	23.10	II	lobectomy	no	190	332
4	Seetha	35	F	50	155	20.81	II	decortication	no	175	320
5	Ananthi	38	F	55	160	21.48	III	bulla excision	no	183	321
6	Chinnaraj	38	M	72	171	24.62	III	mass exccision	no	182	375
7	Savithri	36	F	56	163	21.07	II	decortication	no	192	350
8	Vasantha	40	F	51	165	18.73	II	lobectomy	no	200	370
9	Murugesan	45	M	71	172	23.99	II	lobectomy	no	168	340
10	Pandu	40	M	69	169	24.15	II	lobectomy	no	172	300
11	Vinoth	22	M	66	169	23.10	II	lobectomy	no	180	340
12	Murugesan	40	M	52	167	18.64	II	lobectomy	no	182	345
13	Iyyapan	34	M	67	168	23.73	III	lobectomy	no	192	345
14	Asairaj	35	F	54	159	21.35	II	lobectomy	no	184	355
15	Malar	32	F	55	160	21.48	III	decortication	no	175	320
16	Vinoth	36	M	65	162	24.76	III	decortication	no	173	315
17	Uma rani	37	F	57	163	21.45	II	lobectomy	no	191	340
18	Manickam	40	M	66	170	22.83	III	decortication	no	178	350
19	Gopal	31	M	70	172	23.38	III	decortication	no	176	295
20	Senthil	55	M	66	168	23.38	II	lobectomy	no	186	290
21	Ramya	28	F	52	163	19.57	II	lobectomy	no	200	310
22	Nandagopal	40	M	67	169	23.45	II	lobectomy	no	168	290
23	Sathyamurthy	50	M	66	167	23.66	II	decortication	no	192	315
24	Kuppu	55	F	50	160	19.53	III	lobectomy	no	170	320
25	Raja	25	M	75	171	25.64	III	lobectomy	no	175	330

GROUP F - FENTANYL											
S.NO	**NAME**	**AGE**	**SEX**	**WEIGHT**	**HEIGHT**	**BMI**	**ASA - PS**	**PROCEDURE**	**FAILURE**	**DURATION OF SURGERY (in minutes)**	**DURATION OF ANALGESIA (in minutes)**
1	Mani	38	M	65	169	22.70	II	lobectomy	no	180	110
2	Marimuthu	46	M	60	166	23.43	II	decortication	no	170	99
3	Kesavan	48	M	59	163	22.21	III	lobectomy	no	190	120
4	Amsavalli	56	F	52	160	20.31	III	lobectomy	no	175	110
5	Purushothaman	43	M	73	170	25.25	II	lobectomy	no	183	125
6	Saravanan	39	M	74	172	25.01	II	lobectomy	no	182	95
7	Arumugam	47	M	70	172	23.66	II	decortication	no	192	100
8	Shanmugam	36	M	69	170	23.87	III	decortication	no	200	105
9	Vadivel	49	M	65	165	23.87	III	lobectomy	no	168	110
10	George	57	M	70	168	24.80	III	mass excision	no	172	125
11	Dhivya	30	F	59	163	22.20	II	decortication	no	193	95
12	Kamal	28	M	63	166	22.80	II	lobectomy	no	182	110
13	Irfaan	50	M	66	165	24.24	III	lobectomy	no	192	110
14	Chitra	51	F	58	164	21.56	II	lobectomy	no	184	105
15	Manickam	52	M	60	166	21.77	III	lobectomy	no	165	125
16	Vinoth	48	F	52	159	20.56	II	decortication	no	173	100
17	Arunan	43	M	64	166	23.22	II	decortication	no	191	105
18	Jeeva	53	F	57	164	23.19	II	decortication	no	178	105
19	Lakshmi	40	F	51	165	18.73	II	lobectomy	no	176	124
20	Thilaga	39	F	51	158	20.42	III	decortication	no	184	115
21	Rajesh	34	M	65	170	22.49	III	lobectomy	no	200	100
22	Sriinivasan	37	M	72	173	24.05	III	lobectomy	no	168	120
23	Ponnusamy	36	M	73	174	24.11	II	lobectomy	no	195	110
24	Rajasekar	41	M	69	169	24.15	III	lobectomy	no	170	115
25	Amudha	40	M	73	170	25.25	II	decortication	no	175	112

GROUP D – PULSE RATE															
S.NO	**NAME**	**AGE**	**SEX**	**0 min**	**5 min**	**15 min**	**30 min**	**45 min**	**60 min**	**90 min**	**120 min**	**180 min**	**240 min**	**300 min**	**360 min**
1	Kathirvel	40	M	66	60	58	49	65	65	66	63	60	60	66	78
2	Muthusamy	45	M	74	72	65	64	66	67	68	65	68	69	78	85
3	Kuppan	50	M	70	71	64	58	62	74	76	74	76	72	73	71
4	Seetha	35	F	86	82	72	67	67	67	67	67	68	68	69	72
5	Ananthi	38	F	76	75	64	60	62	70	72	62	63	62	70	70
6	Chinnaraj	38	M	80	82	74	64	64	66	64	59	59	64	62	63
7	Savithri	36	F	82	76	72	65	66	76	83	82	83	82	83	82
8	Vasantha	40	F	74	70	68	61	62	77	76	64	65	64	64	70
9	Murugesan	45	M	80	79	68	67	73	68	68	70	70	66	76	80
10	Pandu	40	M	82	80	72	67	67	72	74	67	68	69	70	77
11	Vinoth	22	M	78	76	72	64	68	73	70	70	70	71	70	70
12	Murugesan	40	M	76	75	65	61	61	65	67	61	62	84	61	71
13	Iyyapan	34	M	82	85	75	66	64	66	68	70	71	69	69	80
14	Asairaj	35	F	82	78	69	66	67	73	69	70	70	67	69	70
15	Malar	32	F	72	70	62	55	55	64	67	64	67	68	70	72
16	Vinoth	36	M	82	82	76	64	64	74	73	64	65	65	68	79
17	Uma rani	37	F	80	78	72	64	68	68	68	70	67	68	68	70
18	Manickam	40	M	74	76	58	69	65	72	76	60	63	65	66	66
19	Gopal	31	M	91	80	70	70	78	80	88	78	70	70	70	78
20	Senthil	55	M	85	84	70	67	70	76	78	66	68	69	70	72
21	Ramya	28	F	86	75	76	76	77	83	80	80	78	76	79	76
22	Nandagopal	40	M	86	80	79	70	78	77	74	71	71	71	72	70
23	Sathyamurthy	50	M	85	84	76	69	71	70	78	80	75	71	71	70
24	Kuppu	55	F	84	82	78	70	72	79	78	71	70	70	73	71
25	Raja	25	M	90	85	84	72	77	72	74	73	75	74	75	70

GROUP F – PULSE RATE											
S.NO	**NAME**	**AGE**	**SEX**	**0 min**	**5 min**	**15 min**	**30 min**	**45 min**	**60 min**	**90 min**	**120 min**
1	Mani	38	M	90	80	76	70	70	83	84	88
2	Marimuthu	46	M	95	90	80	84	85	100	92	90
3	Kesavan	48	M	89	88	84	78	80	86	83	87
4	Amsavalli	56	F	94	90	82	80	85	95	88	87
5	Purushothaman	43	M	84	86	71	70	70	70	70	78
6	Saravanan	39	M	90	93	84	80	81	94	84	86
7	Arumugam	47	M	85	89	78	72	77	76	72	75
8	Shanmugam	36	M	80	80	78	75	85	80	84	85
9	Vadivel	49	M	96	80	82	81	80	84	80	85
10	George	57	M	95	70	75	71	70	74	71	86
11	Dhivya	30	F	78	69	71	70	78	71	71	80
12	Kamal	28	M	72	62	62	61	60	68	62	79
13	Irfaan	50	M	84	75	71	68	70	71	71	88
14	Chitra	51	F	90	84	75	81	76	85	80	85
15	Manickam	52	M	89	88	80	80	90	81	88	90
16	Vinoth	48	F	65	63	61	60	60	58	60	60
17	Arunan	43	M	62	62	58	57	59	59	60	70
18	Jeeva	53	F	90	90	86	80	86	85	82	84
19	Lakshmi	40	F	78	70	68	63	64	70	72	83
20	Thilaga	39	F	83	70	70	69	66	81	74	83
21	Rajesh	34	M	78	69	71	70	70	85	78	80
22	Sriinivasan	37	M	89	76	70	71	72	83	70	76
23	Ponnusamy	36	M	80	78	71	70	71	80	70	88
24	Rajasekar	41	M	76	68	66	65	66	68	64	70
25	Amudha	40	M	75	68	67	66	68	70	66	74

GROUP D – SYSTOLIC BLOOD PRESSURE															
S.NO	**NAME**	**AGE**	**SEX**	**0 min**	**5 min**	**15 min**	**30 min**	**45 min**	**60 min**	**90 min**	**120 min**	**180 min**	**240 min**	**300 min**	**360 min**
1	Kathirvel	40	M	124	104	89	90	104	98	115	100	92	106	110	130
2	Muthusamy	45	M	132	100	104	100	105	102	109	104	100	100	108	128
3	Kuppan	50	M	100	90	92	86	112	95	116	90	100	108	108	93
4	Seetha	35	F	106	95	94	91	84	93	96	94	99	99	94	107
5	Ananthi	38	F	107	109	108	119	91	121	95	125	107	120	121	123
6	Chinnaraj	38	M	101	102	104	101	110	101	96	99	99	89	105	103
7	Savithri	36	F	95	94	95	91	113	90	106	98	99	101	103	98
8	Vasantha	40	F	95	88	90	92	115	90	111	90	94	97	98	110
9	Murugesan	45	M	120	110	100	100	94	100	110	104	104	104	108	138
10	Pandu	40	M	106	100	101	99	114	98	109	102	106	109	109	110
11	Vinoth	22	M	100	90	92	86	117	120	113	123	101	111	108	126
12	Murugesan	40	M	107	109	100	96	106	116	84	127	126	24	126	120
13	Iyyapan	34	M	134	119	116	106	108	105	111	106	107	108	127	126
14	Asairaj	35	F	126	95	94	95	94	91	96	100	89	86	90	101
15	Malar	32	F	127	106	106	93	101	98	85	100	93	100	111	124
16	Vinoth	36	M	100	95	94	95	101	91	90	100	102	118	106	107
17	Uma rani	37	F	120	106	100	106	105	105	86	102	102	110	128	118
18	Manickam	40	M	122	111	113	106	103	109	100	89	89	99	101	103
19	Gopal	31	M	123	118	98	109	97	115	85	116	107	118	125	131
20	Senthil	55	M	141	149	117	108	103	107	99	111	129	126	129	123
21	Ramya	28	F	137	134	118	107	98	118	92	125	111	121	115	137
22	Nandagopal	40	M	116	100	96	96	104	92	112	92	90	110	118	124
23	Sathyamurthy	50	M	130	124	125	100	98	92	87	98	102	108	120	122
24	Kuppu	55	F	129	137	109	101	106	101	91	107	106	104	111	123
25	Raja	25	M	129	137	109	101	106	101	92	107	106	104	111	123

GROUP F – SYSTOLIC BLOOD PRESSURE											
S.NO	**NAME**	**AGE**	**SEX**	**0 min**	**5 min**	**15 min**	**30 min**	**45 min**	**60 min**	**90 min**	**120 min**
1	Mani	38	M	112	129	119	104	128	117	129	124
2	Marimuthu	46	M	121	101	104	102	105	107	127	141
3	Kesavan	48	M	126	122	110	112	116	117	107	133
4	Amsavalli	56	F	125	118	110	90	108	122	106	123
5	Purushothaman	43	M	102	117	98	91	109	112	112	135
6	Saravanan	39	M	130	106	116	110	122	128	97	117
7	Arumugam	47	M	125	125	110	113	130	136	125	138
8	Shanmugam	36	M	133	119	117	115	125	124	107	126
9	Vadivel	49	M	136	124	122	94	122	125	103	130
10	George	57	M	127	120	118	114	119	117	96	130
11	Dhivya	30	F	121	125	110	117	131	134	115	128
12	Kamal	28	M	126	101	104	96	102	100	119	105
13	Irfaan	50	M	128	103	107	95	98	108	100	98
14	Chitra	51	F	108	124	101	94	124	130	123	120
15	Manickam	52	M	123	108	97	95	104	110	120	120
16	Vinoth	48	F	129	122	103	101	135	138	108	125
17	Arunan	43	M	125	124	106	105	125	126	118	128
18	Jeeva	53	F	117	108	108	103	100	100	115	90
19	Lakshmi	40	F	126	121	96	97	115	104	98	98
20	Thilaga	39	F	105	120	95	103	109	105	105	112
21	Rajesh	34	M	103	95	98	90	92	98	120	95
22	Sriinivasan	37	M	118	104	101	96	104	94	97	95
23	Ponnusamy	36	M	124	120	103	98	109	114	91	116
24	Rajasekar	41	M	134	110	108	106	100	103	107	127
25	Amudha	40	M	135	103	90	103	98	97	98	96

GROUP D – DIASTOLIC BLOOD PRESSURE															
S.NO	**NAME**	**AGE**	**SEX**	**0 min**	**5 min**	**15 min**	**30 min**	**45 min**	**60 min**	**90 min**	**120 min**	**180 min**	**240 min**	**300 min**	**360 min**
1	Kathirvel	40	M	78	70	70	60	62	62	75	66	64	70	69	80
2	Muthusamy	45	M	84	70	68	66	63	67	70	64	63	62	70	76
3	Kuppan	50	M	72	66	66	51	75	71	73	66	74	81	77	71
4	Seetha	35	F	65	75	74	64	50	71	61	71	72	71	71	64
5	Ananthi	38	F	81	81	81	83	64	85	62	77	64	83	80	82
6	Chinnaraj	38	M	63	63	54	60	68	57	55	57	50	42	65	58
7	Savithri	36	F	75	74	73	64	68	60	71	59	59	63	64	64
8	Vasantha	40	F	63	56	48	46	72	60	70	63	56	56	50	62
9	Murugesan	45	M	82	70	54	60	58	64	70	63	64	66	70	84
10	Pandu	40	M	60	60	57	54	71	52	70	54	52	55	56	54
11	Vinoth	22	M	70	70	74	55	73	75	71	92	72	76	77	91
12	Murugesan	40	M	81	81	80	63	79	82	52	88	85	85	84	83
13	Iyyapan	34	M	89	84	82	69	79	78	70	80	81	81	88	85
14	Asairaj	35	F	91	75	74	60	73	64	58	74	66	51	66	72
15	Malar	32	F	88	79	80	71	64	81	49	74	71	74	76	86
16	Vinoth	36	M	70	75	74	73	62	64	53	62	64	81	79	81
17	Uma rani	37	F	82	56	60	62	72	62	50	62	62	70	80	70
18	Manickam	40	M	71	66	72	78	61	65	63	40	42	50	47	60
19	Gopal	31	M	82	67	69	68	66	74	51	70	64	73	60	89
20	Senthil	55	M	94	95	65	72	70	65	69	74	80	92	79	83
21	Ramya	28	F	89	91	67	64	68	73	64	60	72	80	79	89
22	Nandagopal	40	M	63	60	54	58	66	60	70	62	48	62	62	82
23	Sathyamurthy	50	M	82	82	78	70	60	60	48	62	72	70	80	82
24	Kuppu	55	F	78	96	75	47	65	48	59	65	78	63	66	73
25	Raja	25	M	80	96	75	47	65	48	64	65	78	63	66	73

GROUP F – DIASTOLIC BLOOD PRESSURE											
S.NO	**NAME**	**AGE**	**SEX**	**0 min**	**5 min**	**15 min**	**30 min**	**45 min**	**60 min**	**90 min**	**120 min**
1	Mani	38	M	70	80	80	62	75	65	85	85
2	Marimuthu	46	M	82	60	75	61	63	72	82	94
3	Kesavan	48	M	85	71	75	75	73	74	68	91
4	Amsavalli	56	F	85	78	73	50	68	72	70	78
5	Purushothaman	43	M	60	71	60	64	65	70	70	93
6	Saravanan	39	M	88	78	68	68	84	80	67	71
7	Arumugam	47	M	83	82	80	72	80	84	82	80
8	Shanmugam	36	M	87	78	74	58	70	68	65	72
9	Vadivel	49	M	90	76	78	71	82	80	63	82
10	George	57	M	85	82	83	73	72	70	62	82
11	Dhivya	30	F	80	82	70	63	86	84	73	92
12	Kamal	28	M	84	60	75	69	61	58	79	58
13	Irfaan	50	M	86	64	78	60	64	62	82	63
14	Chitra	51	F	67	74	60	64	76	84	82	82
15	Manickam	52	M	84	60	63	50	62	60	80	72
16	Vinoth	48	F	88	80	65	72	84	85	71	82
17	Arunan	43	M	86	72	67	61	71	74	75	73
18	Jeeva	53	F	75	64	67	54	58	66	70	50
19	Lakshmi	40	F	86	83	65	62	75	70	67	65
20	Thilaga	39	F	70	80	66	68	70	63	63	80
21	Rajesh	34	M	65	64	66	62	64	68	80	63
22	Sriinivasan	37	M	78	63	78	58	60	60	67	61
23	Ponnusamy	36	M	84	81	64	65	70	71	58	75
24	Rajasekar	41	M	90	75	70	68	63	61	68	80
25	Amudha	40	M	100	70	62	67	67	63	67	67

GROUP D – MEAN ARTERIAL PRESSURE															
S.NO	**NAME**	**AGE**	**SEX**	**0 min**	**5 min**	**15 min**	**30 min**	**45 min**	**60 min**	**90 min**	**120 min**	**180 min**	**240 min**	**300 min**	**360 min**
1	Kathirvel	40	M	93	86	80	70	76	74	88	77	80	82	102	96
2	Muthusamy	45	M	100	80	82	77	77	79	83	77	72	74	83	93
3	Kuppan	50	M	63	74	73	63	87	78	87	74	83	90	87	78
4	Seetha	35	F	73	82	81	73	61	78	73	79	81	80	79	75
5	Ananthi	38	F	90	90	90	95	73	97	73	87	75	95	90	91
6	Chinnaraj	38	M	72	72	70	69	82	67	69	68	64	55	76	70
7	Savithri	36	F	82	81	80	69	83	76	83	69	70	72	74	74
8	Vasantha	40	F	74	66	62	61	86	70	84	72	68	70	66	78
9	Murugesan	45	M	95	83	70	69	73	76	83	77	77	79	83	102
10	Pandu	40	M	76	73	72	69	85	70	83	70	70	73	74	73
11	Vinoth	22	M	80	81	78	65	88	83	85	104	82	88	87	103
12	Murugesan	40	M	90	90	89	74	88	93	63	101	99	98	98	95
13	Iyyapan	34	M	104	96	93	82	88	87	84	89	90	90	101	99
14	Asairaj	35	F	103	82	81	71	80	73	71	83	74	63	74	82
15	Malar	32	F	101	88	89	76	78	90	61	83	78	83	88	99
16	Vinoth	36	M	80	82	81	71	70	73	65	74	78	93	88	90
17	Uma rani	37	F	95	73	73	77	83	76	62	75	75	83	96	86
18	Manickam	40	M	81	79	84	74	78	81	75	79	79	74	76	78
19	Gopal	31	M	91	81	76	75	78	85	62	81	75	83	77	101
20	Senthil	55	M	110	117	77	74	81	82	79	84	91	101	92	94
21	Ramya	28	F	104	103	81	75	78	83	73	77	81	90	88	104
22	Nandagopal	40	M	81	73	68	71	79	71	84	72	75	78	81	96
23	Sathyamurthy	50	M	98	96	94	80	73	66	61	74	82	83	93	95
24	Kuppu	55	F	95	100	86	66	79	68	70	74	86	72	79	86
25	Raja	25	M	94	100	86	66	79	68	73	74	86	72	79	86

GROUP F – MEAN ARTERIAL PRESSURE											
S.NO	**NAME**	**AGE**	**SEX**	**0 min**	**5 min**	**15 min**	**30 min**	**45 min**	**60 min**	**90 min**	**120 min**
1	Mani	38	M	84	91	93	76	89	77	100	95
2	Marimuthu	46	M	95	69	88	69	77	81	97	110
3	Kesavan	48	M	99	81	87	87	83	84	81	102
4	Amsavalli	56	F	98	91	85	61	81	89	82	93
5	Purushothaman	43	M	74	81	73	73	81	81	84	106
6	Saravanan	39	M	102	86	84	82	93	93	77	81
7	Arumugam	47	M	97	96	90	83	96	101	96	100
8	Shanmugam	36	M	102	92	88	86	88	87	79	90
9	Vadivel	49	M	105	92	93	70	95	95	76	98
10	George	57	M	99	95	97	85	78	86	73	98
11	Dhivya	30	F	94	96	83	88	101	101	87	104
12	Kamal	28	M	98	69	89	74	69	70	92	77
13	Irfaan	50	M	100	74	91	70	74	82	95	72
14	Chitra	51	F	81	91	74	71	92	99	96	97
15	Manickam	52	M	93	76	74	64	76	77	93	88
16	Vinoth	48	F	102	94	78	75	101	103	83	96
17	Arunan	43	M	99	89	80	83	89	91	89	91
18	Jeeva	53	F	89	79	81	69	72	75	85	63
19	Lakshmi	40	F	82	96	83	75	88	76	77	76
20	Thilaga	39	F	78	93	76	75	83	77	77	91
21	Rajesh	34	M	91	74	76	71	73	78	93	74
22	Sriinivasan	37	M	97	77	92	71	81	71	77	72
23	Ponnusamy	36	M	105	94	77	77	83	85	69	89
24	Rajasekar	41	M	101	87	84	79	75	75	81	96
25	Amudha	40	M	110	81	77	73	77	74	77	77

GROUP D – SIDE EFFECTS										
S.NO	**NAME**	**AGE**	**SEX**	**BRADYCARDIA**	**HYPOTENSION**	**NAUSEA**	**VOMITING**	**DRY MOUTH**	**PRURITUS**	**RESPIRATORY DEPRESSION**
1	Kathirvel	40	M	Yes	No	No	No	Yes	No	No
2	Muthusamy	45	M	No	No	No	No	No	No	No
3	Kuppan	50	M	No	No	No	No	No	No	No
4	Seetha	35	F	No	No	No	No	No	No	No
5	Ananthi	38	F	No	No	No	No	No	No	No
6	Chinnaraj	38	M	No	No	No	No	No	No	No
7	Savithri	36	F	No	No	No	No	No	No	No
8	Vasantha	40	F	No	No	Yes	No	Yes	No	No
9	Murugesan	45	M	No	No	No	No	No	No	No
10	Pandu	40	M	No	No	No	No	No	No	No
11	Vinoth	22	M	No	No	No	No	No	No	No
12	Murugesan	40	M	No	No	No	No	No	No	No
13	Iyyapan	34	M	No	No	No	No	No	No	No
14	Asairaj	35	F	No	Yes	No	No	No	No	No
15	Malar	32	F	No	No	Yes	No	No	No	No
16	Vinoth	36	M	No	No	No	No	No	No	No
17	Uma rani	37	F	No	No	No	No	No	No	No
18	Manickam	40	M	No	No	No	No	No	No	No
19	Gopal	31	M	No	No	No	No	No	No	No
20	Senthil	55	M	No	No	No	No	No	No	No
21	Ramya	28	F	No	No	No	No	No	No	No
22	Nandagopal	40	M	No	No	No	No	No	No	No
23	Sathyamurthy	50	M	No	No	No	No	Yes	No	No
24	Kuppu	55	F	No	No	No	No	No	No	No
25	Raja	25	M	No	No	No	No	No	No	No

GROUP F – SIDE EFFECTS										
S.NO	**NAME**	**AGE**	**SEX**	**BRADYCARDIA**	**HYPOTENSION**	**NAUSEA**	**VOMITING**	**DRY MOUTH**	**PRURITUS**	**RESPIRATORY DEPRESSION**
1	Mani	38	M	No	No	No	No	No	No	No
2	Marimuthu	46	M	No	No	No	No	No	No	No
3	Kesavan	48	M	No	No	No	No	No	No	No
4	Amsavalli	56	F	No	No	No	No	No	No	No
5	Purushothaman	43	M	No	No	Yes	Yes	No	Yes	No
6	Saravanan	39	M	No	No	No	No	No	No	No
7	Arumugam	47	M	No	No	No	No	No	No	No
8	Shanmugam	36	M	No	No	No	No	No	No	No
9	Vadivel	49	M	No	No	Yes	No	No	No	No
10	George	57	M	No	No	No	No	No	No	No
11	Dhivya	30	F	No	No	No	No	No	No	No
12	Kamal	28	M	No	No	No	No	No	No	No
13	Irfaan	50	M	No	No	Yes	Yes	No	No	No
14	Chitra	51	F	No	No	No	No	No	No	No
15	Manickam	52	M	No	No	No	No	No	No	No
16	Vinoth	48	F	No	No	No	No	No	No	No
17	Arunan	43	M	No	No	No	No	No	No	No
18	Jeeva	53	F	No	No	No	No	No	No	No
19	Lakshmi	40	F	No	No	No	No	No	Yes	No
20	Thilaga	39	F	No	No	No	No	No	No	No
21	Rajesh	34	M	No	No	No	No	No	No	No
22	Sriinivasan	37	M	No	No	No	No	No	No	No
23	Ponnusamy	36	M	No	No	No	No	No	No	No
24	Rajasekar	41	M	No	No	No	No	No	No	No
25	Amudha	40	M	No	Yes	No	No	No	No	No

GROUP D – VISUAL ANALOGUE SCORE											
S.NO	**NAME**	**AGE**	**SEX**	**30 min**	**60 min**	**90 min**	**120 min**	**180 min**	**240 min**	**300 min**	**360 min**
1	Kathirvel	40	M	0	0	0	1	1	2	2	4
2	Muthusamy	45	M	0	0	0	1	2	2	3	4
3	Kuppan	50	M	0	1	1	2	2	3	3	4
4	Seetha	35	F	0	0	0	1	2	2	3	4
5	Ananthi	38	F	0	0	0	2	2	3	3	4
6	Chinnaraj	38	M	0	0	0	1	1	2	3	3
7	Savithri	36	F	0	0	1	1	2	3	3	4
8	Vasantha	40	F	0	1	1	1	2	2	3	3
9	Murugesan	45	M	0	1	1	2	2	3	4	4
10	Pandu	40	M	0	1	1	1	2	2	4	4
11	Vinoth	22	M	0	1	1	2	2	2	3	4
12	Murugesan	40	M	0	0	0	1	2	2	3	4
13	Iyyapan	34	M	0	1	1	2	3	3	3	4
14	Asairaj	35	F	0	0	0	1	2	2	3	4
15	Malar	32	F	0	0	1	1	1	2	3	4
16	Vinoth	36	M	0	0	0	1	1	2	3	4
17	Uma rani	37	F	0	0	1	1	2	2	3	4
18	Manickam	40	M	0	0	1	0	1	2	2	4
19	Gopal	31	M	0	0	1	1	2	2	4	4
20	Senthil	55	M	0	0	1	2	2	2	4	4
21	Ramya	28	F	0	1	1	2	2	2	3	4
22	Nandagopal	40	M	0	0	0	0	1	3	4	4
23	Sathyamurthy	50	M	0	0	1	2	2	3	4	4
24	Kuppu	55	F	0	1	1	1	1	3	3	4
25	Raja	25	M	0	0	0	1	2	2	3	4

GROUP F – VISUAL ANALOGUE SCORE									
S.NO	**NAME**	**AGE**	**SEX**	**15 min**	**30 min**	**45 min**	**60 min**	**90 min**	**120 min**
1	Mani	38	M	0	2	2	2	2	4
2	Marimuthu	46	M	0	1	1	2	3	4
3	Kesavan	48	M	0	1	1	2	2	3
4	Amsavalli	56	F	0	0	1	2	2	4
5	Purushothaman	43	M	0	1	1	2	2	3
6	Saravanan	39	M	0	2	2	3	3	4
7	Arumugam	47	M	0	1	2	2	3	4
8	Shanmugam	36	M	0	1	1	2	3	4
9	Vadivel	49	M	0	1	1	2	2	4
10	George	57	M	0	2	2	2	2	3
11	Dhivya	30	F	0	2	2	2	3	4
12	Kamal	28	M	0	1	1	2	2	4
13	Irfaan	50	M	0	2	2	2	2	4
14	Chitra	51	F	0	1	1	3	3	4
15	Manickam	52	M	0	1	1	2	2	3
16	Vinoth	48	F	0	2	2	2	3	4
17	Arunan	43	M	0	2	2	2	3	4
18	Jeeva	53	F	0	1	1	2	2	4
19	Lakshmi	40	F	0	0	0	2	2	3
20	Thilaga	39	F	0	1	1	2	2	4
21	Rajesh	34	M	0	0	0	2	3	4
22	Sriinivasan	37	M	0	1	1	2	2	3
23	Ponnusamy	36	M	0	0	0	1	2	4
24	Rajasekar	41	M	0	1	1	1	2	4
25	Amudha	40	M	0	1	1	2	3	4

GROUP D – SEDATION SCORE													
S.NO	**NAME**	**AGE**	**SEX**	**15 min**	**30 min**	**45 min**	**60 min**	**90 min**	**120 min**	**180 min**	**240 min**	**300 min**	**360 min**
1	Kathirvel	40	M	3	3	3	3	3	2	2	2	1	1
2	Muthusamy	45	M	3	3	3	3	3	2	2	2	1	1
3	Kuppan	50	M	3	3	3	3	3	2	2	1	1	1
4	Seetha	35	F	3	3	3	3	3	2	2	2	2	1
5	Ananthi	38	F	3	3	3	3	3	2	2	1	1	1
6	Chinnaraj	38	M	3	3	3	3	2	3	3	2	2	2
7	Savithri	36	F	3	3	3	3	2	2	2	1	1	1
8	Vasantha	40	F	3	3	3	3	2	2	2	2	1	1
9	Murugesan	45	M	3	2	2	2	2	2	2	1	1	1
10	Pandu	40	M	3	3	3	3	3	1	2	1	1	1
11	Vinoth	22	M	3	2	2	2	2	2	1	1	1	1
12	Murugesan	40	M	3	3	3	2	2	2	2	2	1	1
13	Iyyapan	34	M	3	3	3	3	3	2	2	1	1	1
14	Asairaj	35	F	3	3	3	3	3	2	2	1	1	1
15	Malar	32	F	2	2	2	2	2	2	2	2	1	1
16	Vinoth	36	M	3	3	3	3	3	2	2	2	1	1
17	Uma rani	37	F	3	2	2	2	2	2	1	1	1	1
18	Manickam	40	M	3	3	3	2	2	2	2	2	1	1
19	Gopal	31	M	3	3	3	2	2	2	2	1	1	1
20	Senthil	55	M	3	3	3	3	2	2	2	2	1	1
21	Ramya	28	F	3	3	3	2	2	2	2	1	1	1
22	Nandagopal	40	M	3	3	3	3	3	2	2	1	1	1
23	Sathyamurthy	50	M	3	3	3	3	3	2	2	1	1	1
24	Kuppu	55	F	3	3	3	2	2	2	2	1	1	1
25	Raja	25	M	3	3	3	2	2	2	2	2	1	1

GROUP F – SEDATION SCORE									
S.NO	**NAME**	**AGE**	**SEX**	**15 min**	**30 min**	**45 min**	**60 min**	**90 min**	**120 min**
1	Mani	38	M	1	1	1	1	1	1
2	Marimuthu	46	M	2	1	1	1	1	1
3	Kesavan	48	M	1	1	1	1	1	1
4	Amsavalli	56	F	2	1	1	1	1	1
5	Purushothaman	43	M	1	1	1	1	1	1
6	Saravanan	39	M	2	1	1	1	1	1
7	Arumugam	47	M	2	1	1	1	1	1
8	Shanmugam	36	M	2	1	1	1	1	1
9	Vadivel	49	M	2	1	1	1	1	1
10	George	57	M	2	1	1	1	1	1
11	Dhivya	30	F	2	1	1	1	1	1
12	Kamal	28	M	2	1	1	1	1	1
13	Irfaan	50	M	2	1	1	1	1	1
14	Chitra	51	F	2	2	2	1	1	1
15	Manickam	52	M	2	2	2	1	1	1
16	Vinoth	48	F	2	1	1	1	1	1
17	Arunan	43	M	2	1	1	1	1	1
18	Jeeva	53	F	2	1	1	1	1	1
19	Lakshmi	40	F	2	1	1	1	1	1
20	Thilaga	39	F	2	1	1	1	1	1
21	Rajesh	34	M	2	2	2	1	1	1
22	Sriinivasan	37	M	2	1	1	1	1	1
23	Ponnusamy	36	M	2	1	1	1	1	1
24	Rajasekar	41	M	2	2	2	1	1	1
25	Amudha	40	M	2	2	1	1	1	1

GROUP D – RESPIRATORY RATE													
S.NO	**NAME**	**AGE**	**SEX**	**15 min**	**30 min**	**45 min**	**60 min**	**90 min**	**120 min**	**180 min**	**240 min**	**300 min**	**360 min**
1	Kathirvel	40	M	16	18	15	16	14	15	15	17	19	17
2	Muthusamy	45	M	14	16	13	12	14	12	14	17	16	14
3	Kuppan	50	M	18	17	15	18	17	16	18	20	18	16
4	Seetha	35	F	14	15	16	16	15	17	15	18	19	15
5	Ananthi	38	F	16	17	16	18	16	12	15	16	18	15
6	Chinnaraj	38	M	18	17	15	16	16	15	17	18	19	17
7	Savithri	36	F	14	16	15	12	13	15	16	14	14	16
8	Vasantha	40	F	13	15	15	17	14	12	13	15	16	14
9	Murugesan	45	M	17	15	15	16	17	15	17	18	17	15
10	Pandu	40	M	15	17	18	16	18	16	16	18	17	18
11	Vinoth	22	M	14	13	16	15	17	16	18	17	16	15
12	Murugesan	40	M	15	16	14	18	17	16	17	19	16	18
13	Iyyapan	34	M	15	15	16	18	16	14	17	18	18	17
14	Asairaj	35	F	17	16	17	15	18	16	17	18	14	15
15	Malar	32	F	15	17	16	18	16	17	16	15	17	16
16	Vinoth	36	M	12	15	16	15	15	17	16	16	14	13
17	Uma rani	37	F	14	14	13	15	16	13	16	15	14	15
18	Manickam	40	M	15	17	15	18	14	15	16	18	19	17
19	Gopal	31	M	16	18	15	16	14	16	14	16	18	19
20	Senthil	55	M	15	17	18	15	16	14	17	18	16	15
21	Ramya	28	F	12	13	15	13	12	13	15	16	14	12
22	Nandagopal	40	M	13	15	13	14	16	11	13	14	17	15
23	Sathyamurthy	50	M	15	16	14	16	13	17	14	15	16	15
24	Kuppu	55	F	16	18	16	17	18	20	19	16	17	16
25	Raja	25	M	14	13	12	11	14	15	14	13	14	15

GROUP F - RESPIRATORY RATE									
S.NO	**NAME**	**AGE**	**SEX**	**15 min**	**30 min**	**45 min**	**60 min**	**90 min**	**120 min**
1	Mani	38	M	14	16	14	16	15	17
2	Marimuthu	46	M	16	17	16	14	18	16
3	Kesavan	48	M	13	14	13	15	13	16
4	Amsavalli	56	F	14	13	15	13	16	16
5	Purushothaman	43	M	15	15	14	13	15	16
6	Saravanan	39	M	13	12	14	13	14	13
7	Arumugam	47	M	13	15	13	15	14	14
8	Shanmugam	36	M	14	13	14	15	13	16
9	Vadivel	49	M	16	17	14	16	18	19
10	George	57	M	16	15	16	14	16	17
11	Dhivya	30	F	14	13	14	15	13	15
12	Kamal	28	M	15	15	14	16	14	15
13	Irfaan	50	M	16	15	15	17	14	13
14	Chitra	51	F	15	17	13	14	16	15
15	Manickam	52	M	16	14	16	14	14	15
16	Vinoth	48	F	12	15	13	12	11	13
17	Arunan	43	M	13	12	13	12	15	14
18	Jeeva	53	F	15	17	14	15	14	16
19	Lakshmi	40	F	15	14	14	13	15	14
20	Thilaga	39	F	13	12	13	11	13	15
21	Rajesh	34	M	12	13	12	14	16	16
22	Sriinivasan	37	M	13	14	13	16	14	15
23	Ponnusamy	36	M	13	16	14	13	14	13
24	Rajasekar	41	M	14	13	12	11	13	15
25	Amudha	40	M	15	16	14	12	13	14

PROFORMA

“PROSPECTIVE, RANDOMIZED COMPARATIVE STUDY ON EFFECTS OF ADDING DEXMEDITOMIDINE AND FENTANYL TO EPIDURAL BUPIVACAINE (0.125%) ON POST OPERATIVE ANALGESIA IN PATIENTS UNDERGOING THORACOTOMY"

Name: Age: Sex:

I.P.No:

Diagnosis:

Surgery Planned:

Preoperative Assessment:

History:

Co-Morbid Illness & Treatment Details:

Effort Tolerance- _____ Mets

H/O Previous Surgery:

GENERAL EXAMINATION:

Height: Weight: BMI:

Anaemia Jaundice

Pulse BP CVS RS Spine

INVESTIGATIONS:

BT: CT:

Blood Grouping & Typing:

Blood Sugar: Urea:

Creatinine: ECG: CXR:

PFT:

EPIDURAL CATHETERISATION:

Position: Space: Needle:

Size: Median/Paramedian

Induction:

Proceed with Surgery:

Study Drug Administration:

Extubation:

POST OP VITAL PARAMETERS:

TIME	HR	SBP	DBP	MAP	SPO2	RR	VAS	Sedation
0 min								
5 min								
15 min								
30 min								
45 min								
60 min								
90 min								
120								

min								
180 min								
240 min								
300 min								
360 min								

Post OP:

Rescue Analgesic Time

Side Effects:

Hypotension

Urinary Retention

Bradycardia

Respiratory Depression

Nausea, Vomiting

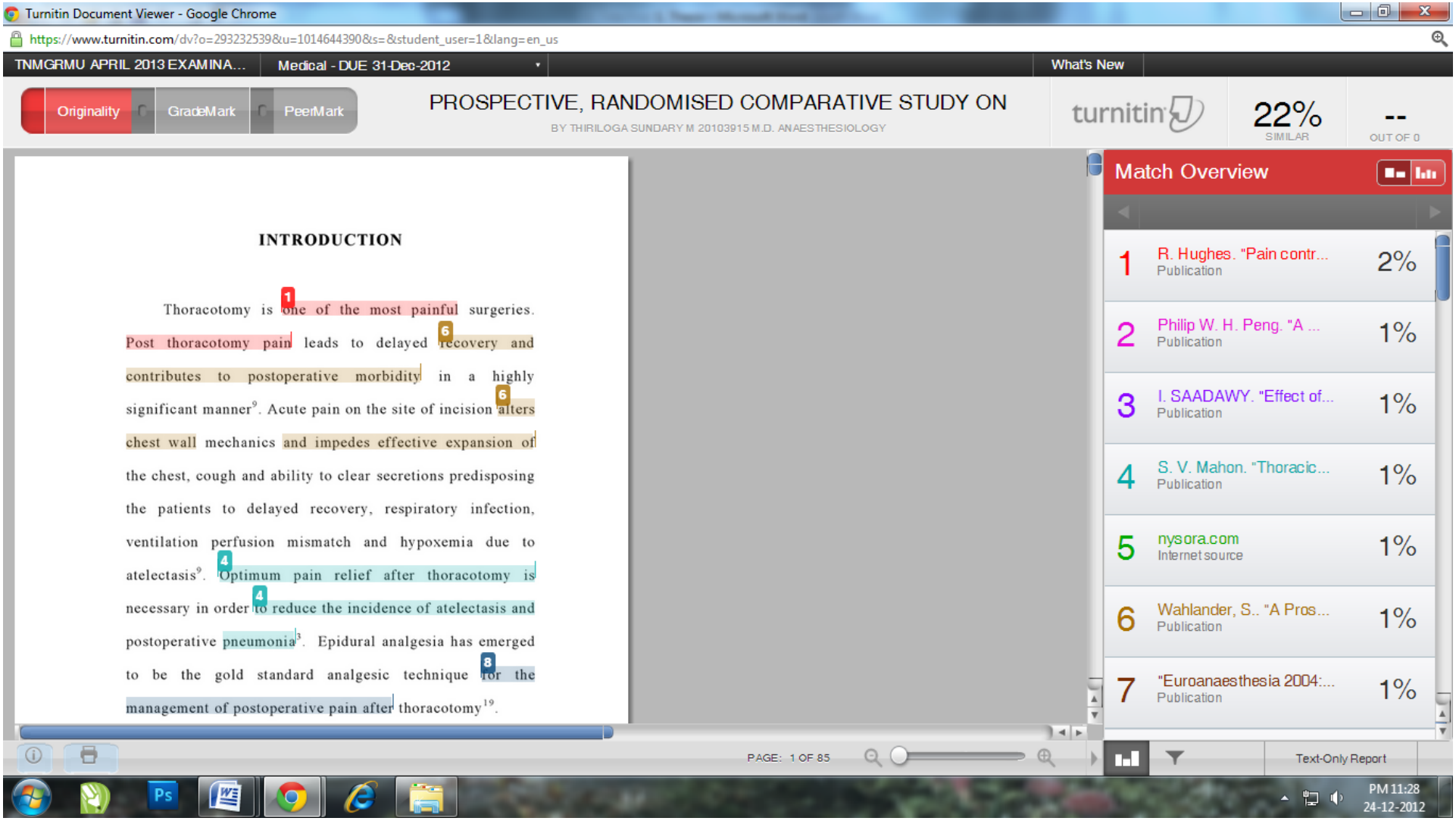
Dry Mouth

Drugs:

INJ. Ephedrine ___ mg Time:

INJ. Atropine __ mg Time:

ANTIPLAGARISM SCREEN SHOT



PATIENT INFORMATION FORM

Name of the Investigator: Dr.M. Thiriloga Sundary
Name of the Participant:

Title: Prospective randomized comparative study on the effects of adding dexmedetomidine and fentanyl to epidural bupivacaine (0.125%) on post operative analgesia in patients undergoing thoracotomy.

You are invited to take part in this research study conducted in Madras Medical College and Rajiv Gandhi Government General Hospital. We have got approval from the IEC. You are ask to participate in the study because you satisfy the eligibility criteria.

PURPOSE OF RESEARCH

We want to compare the safe and efficacy of epidural dexmedetomidine and epidural fentanyl when given along with bupivacaine for post operative pain relief after thorocotomy.

These drugs when administered via epidural route provide post operative pain relief and also avoid usage of other systemic analgesic which might be harmful to you.

STUDY DESIGN

Patients will be divided into two groups.

At end of surgery 1st group will receive dexmedetomidine plus bupivacaine epidurally. 2nd group will receive fentanyl plus bupivacaine epidurally.

After administering the drug, patient's heart rate, blood pressure, analgesic efficacy of the drug and several other parameters will be monitored.

BENEFITS

It has been observed from previous studies that these epidurally administered drugs provide good post operative pain relief. This reduces usage of other analgesics drugs and thereby avoids their side effects.

DISCOMFORTS AND RISKS

There might be reduction in heart rate and blood pressure. For reduction in heart rate atropine will be given. For reduction in blood pressure ephedrine will be given.

This intervention has been shown to be well tolerated as indicated by previous studies. Which group you will be assigned to depends entirely on chance and if you do not want to participate you will have the alternative of getting the standard treatment and your safety is our prime consent.

Witness Name Participants Name

Signature Signature

PATIENT CONSENT FORM

Study title: Prospective, randomized comparative study on effect of adding dexmedetomidine and fentanyl to epidural bupivacaine (0.125%) on postoperative analgesia in patients undergoing thoracotomy procedures.

Study centre: Institute of Anaesthesiology and Critical Care
Madras Medical College & Govt. General Hospital
Chennai - 600003

Participant name: Age: Sex:
I.P.No:

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction.

I have been explained about the pitfall in the procedure. I have been explained about the safety, advantage and disadvantage of the technique.

I understand that my participation in the study is voluntary and that I am free to withdraw at anytime without giving any reason.

I understand that investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to current study and any further research that may be conducted in relation to it, even if I withdraw from the study. I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study.

Time:

Date:

Signature / Thumb impression of patient

Place:

Patient name:

Signature of the investigator:

Name of the investigator: